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RÔLE OF THE CEREBELLUM IN POSTURAL CONTRACTIONS

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In a recent investigation of the responses to stimulation of the interior of the cerebellum in the normal monkey,[1] a medially situated cerebellar system was found, each side of which is capable of exerting a pronounced and rather stereotyped influence on the tonus of the muscles of the eyes, neck, trunk and limbs on both sides of the body. The response of this system to electrical stimulation is ordinarily biphasic, one phase of the reaction being manifest during stimulation and the other appearing as a rebound at the conclusion of stimulation.

The rebound phase of the reaction was always excitatory, leading to contraction of the muscles, producing deviation of the eyes and concavity of the body axis to the side opposite the cerebellar stimulation and also to contraction of the muscles of the limbs, which was reciprocal on the two sides of the body in that the ipsilateral extensor muscles and the contralateral flexor muscles of the limbs were excited. We are unable to say whether there was also rebound inhibition of the antagonists of these groups of muscles. The rebound contractions were marked and rigid and persisted for minutes.

Cerebellar stimulation during a rebound contraction promptly caused its relaxation and, in some instances, led to reciprocal contraction of the antagonists of the muscles contracting in the rebound. At the conclusion of stimulation the rebound posture was once more briskly assumed.

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1. Magoun, H. W.; Hare, W. K., and Ranson, S. W.: Electrical Stimulation of the Interior of the Cerebellum in the Monkey, Am. J. Physiol. **112**:329, 1935.

This medially situated cerebellar system has been identified, in all its particulars, in the normal cat,[2] and in this animal it has not been found to be appreciably affected by decerebration, either in front of or behind the red nucleus, other than to yield more marked effects to stimulation in the decerebrate animal.

It seems clear that this system is the one responsible for the classic cerebellar function of inhibition of decerebrate rigidity, and Bremer[3] must be accredited with its first recognition under fairly normal conditions of tonus, as he produced many of its effects in the standing thalamic pigeon and cat.

The present report is concerned with an investigation of some general features of the reactions to stimulation of this system in the medial portion of the interior of the cerebellum in the cat. Effort has been directed: (1) to a study of the part which tonic reflexes play in the prolonged rebound contractions following cessation of cerebellar stimulation and (2) to a study of cerebellar release effects and the question of their relationship to the rebound contractions.

METHODS

A total of twenty-eight cats were employed in two series of experiments. In the first series of thirteen animals, under light anesthesia induced with pentobarbital sodium (from 12 to 19 mg. per kilogram of body weight), the duration of rebound contractions following cessation of cerebellar stimulation was studied, after elimination of tonic reflexes. In all the thirteen animals the right forelimb was deafferented, under aseptic precautions, by section of the posterior roots, from the third or fourth cervical to the fourth thoracic inclusive, from two to four weeks before the experiment. In six animals, eight weeks prior to stimulation, bilateral labyrinthectomy had been performed, using the de Kleyn method (Magnus[4]). Just before the experiment, the opposite, or left, forelimb was denervated in eleven of the thirteen animals by section of its brachial plexus, and during the experiment in twelve of the thirteen animals the nerve supply of the hindlimbs was eliminated from consideration by section of the lower thoracic portion of the spinal cord. Stimulation of the cerebellum in these animals was performed as a routine, with the animals in the hanging position, the duration of rebound contractions being determined by observation and light manipulation and a stopwatch. No contraction of less than five seconds' duration has been considered in this study.

2. Hare, W. K.; Magoun, H. W., and Ranson, S. W.: Electrical Stimulation of the Interior of the Cerebellum in the Decerebrate Cat, Am. J. Physiol. **117**:261, 1936; Localization Within the Cerebellum of Reactions to Faradic Cerebellar Stimulation, J. Comp. Neurol., to be published. Ingersoll, E. H.; Magoun, H. W., and Ranson, S. W.: The Spinal Paths for Responses to Cerebellar Stimulation, Am. J. Physiol. **117**:267, 1936.

3. Bremer, F.: Le cervelet, in Roger, G. H., and Binet, Leon: Traité de physiologie normale et pathologique, Paris, Masson & Cie, 1935, vol. 10.

4. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924, p. 274.

Stimulation of the interior of the cerebellum was performed in these animals with the aid of the Horsley-Clarke stereotaxic instrument, the use of which has been described elsewhere (Ranson[5]). The cerebellum was exposed by incision of the skin, reflection of the dorsal muscles of the neck from the posterior surface of the occipital bone and the enlargement dorsally of the foramen magnum. The Horsley-Clarke instrument was adjusted to the animal's head, and cerebellar stimulation was performed along electrode punctures in a horizontal plane, the electrodes entering the cerebellum from its caudal surface, after removal of the dura. The two electrodes, represented by the exposed tips of otherwise enameled lengths of fine nichrome wire, were separated from one another by a distance of 1 mm., along the axis of the "needle" produced by cementing the two wires together. The current was supplied by one dry cell attached to a Harvard inductorium, the secondary coil of which was set at 9 cm.

The needle-like electrodes were inserted into the cerebellum to the desired location, where they were halted and stimulation was applied. After the response was recorded in systematic notes, the electrodes were inserted 1 mm. farther, and stimulation was again applied, and so on, until the puncture was completed. The electrodes were then withdrawn from the cerebellum and moved 1 mm. to the right or to the left in the same horizontal plane, and a similar puncture, with its series of stimuli, was made. On completion of a horizontal row of such punctures, the electrodes were lowered 2 mm., and a similar row was undertaken. In this way, as much of the interior of the cerebellum as was desired could be systematically explored by stimulation at intervals of 1 mm. throughout its substance. Alternating horizontal levels could be explored in different animals. By starting dorsally and progressing ventrally in each animal and by beginning each puncture caudally and carrying it rostrally, the intact efferent connections always lay ahead of every point of stimulation.

At the conclusion of stimulation the brain was injected in situ through the carotid arteries, and a block, including the region explored, was removed, embedded, cut serially in a plane parallel to the rows of punctures and stained for microscopic examination by the Weil method. Each puncture could be identified in the sections as a fine line of hemorrhage; by measuring back from the anterior end of each puncture, after calculating for shrinkage, the location of each point of stimulation could be determined and a correlation made with the response obtained. The localization of the reactive points was first indicated for each animal on projection drawings through the explored area, responses being differentiated by symbols. All the results were then transferred to a standard series of six horizontal levels through the cerebellum of the cat and are shown in figure 1.

In a second series of fifteen normal animals, under light anesthesia induced with pentobarbital sodium, experiments as controls were performed on cerebellar release effects. In four animals the cerebellum was completely extirpated. In five animals the interior of the cerebellum was repeatedly punctured in the manner previously described, but without electrical stimulation. In three animals the medial cerebellar nuclei were undercut by a fine wire ground to a knife-edge and oriented in the horizontal electrode carrier of the Horsley-Clarke instrument. In three animals the interior of each side of the medial portions of the cerebellum

5. Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. **38**:534, 1934.

was narcotized by the injection of from 0.18 to 0.24 cc. of a 0.5 per cent solution of cocaine hydrochloride, in two cases, and of a like amount of an 8 per cent solution of cocaine hydrochloride, in one case. Injection was performed with a tuberculin syringe, through a long, 20 gage syringe needle oriented in the horizontal electrode carrier of the Horsley-Clarke instrument.

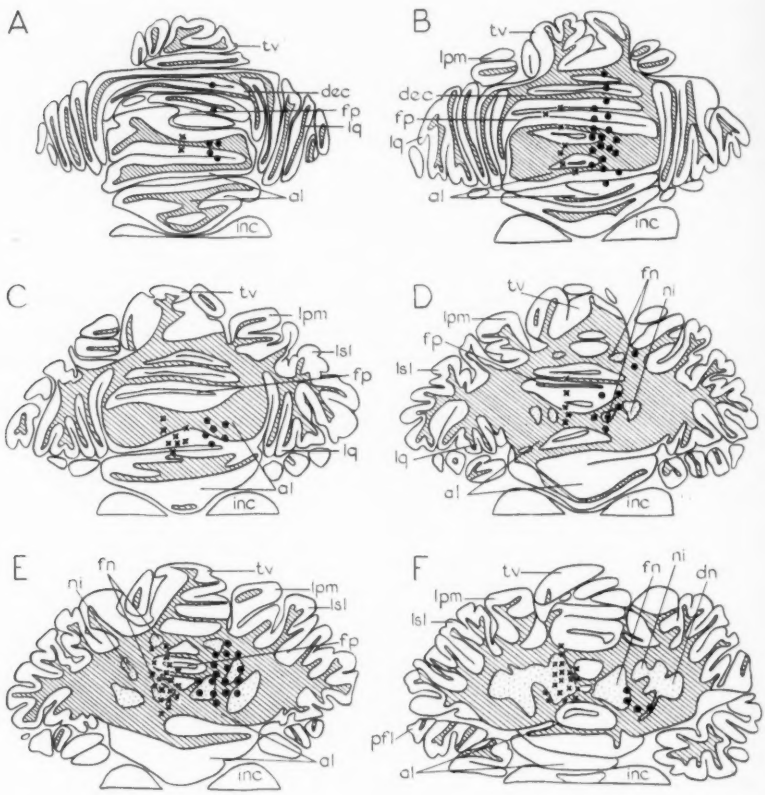

Fig. 1.—Drawings showing localization within the cerebellum of points at which stimulation yielded the reactions of the right forelimb obtained from the series of deafferented animals. Circles represent points at which stimulation was followed by a rebound extension of the right forelimb. Crosses denote points at which stimulation was followed by a rebound flexion of the right forelimb. The six horizontal levels through the cerebellum extend serially from the most dorsal plane, *A*, to the most ventral plane, *F*, the distance between *A* and *F* being 4 mm. In each of these levels the posterior aspect of the cerebellum is directed toward the top of the page. Two animals of the series were stimulated in plane *A;* five in plane *B;* four, in plane *C;* two, in plane *D;* five in plane *E*, and five, in plane *F*.

The following abbreviations are used in this figure: *al* indicates lobus anterior; *dec*, the declive; *dn*, the dentate nucleus; *fn*, the fastigial nucleus; *fp*, fissura prima; *inc*, the inferior colliculus; *lpm*, lobulus paramedianus; *lq*, lobulus quadrangularis; *lsl*, lobulus semilunaris; *ni*, nucleus interpositus; *pfl*, paraflocculus, and *tv*, tuber vermis.

OBSERVATIONS

Rebound Following Cerebellar Stimulation.—The rebound phase of reactions to cerebellar stimulation was recognized by Bechterew,[6] Bremer,[7] Miller and Laughton [8] and Denny-Brown, Eccles and Liddell.[9] Bremer expressed the opinion that it represented a combination of tonic labyrinthine and myotatic reflexes; Miller and Laughton suggested its homology with cerebellar release effects, and Denny-Brown, Eccles and Liddell called it a manifestation of cerebellar activity, which also appears to have been the implication of Bechterew.

The "gradual subsidence" of the rebound contractions following cerebellar stimulation was referred to by Miller and Laughton;[8] examples of this are shown in their myograms and in those published by Bremer.[7] We have called attention to the fact that these rebound contractions commonly persist for five minutes or longer after cessation of even a brief stimulation of the cerebellum in the normal monkey,[1] and we have observed comparable effects in the cat.[2] The question naturally arises as to what activity is responsible for the long-lasting discharge of efferent centers which underlies the maintenance of these postures.

The possibility that tonic reflexes provide the mechanism for this activity suggested itself, and it was decided to investigate the rôle which afferent impulses play in these rebounds, in particular the afferent impulses from the muscles of the limbs and from the labyrinths, which are commonly thought to play an important part in all tonic contractions.

In the first series, consisting of thirteen specially prepared animals, the duration of the rebound contraction was studied in a deafferented forelimb after fixation of the neck in the midline, denervation of the opposite forelimb and elimination of the hindlimbs by section of the lower thoracic portion of the spinal cord. In six of these animals bilateral labyrinthectomy had also been performed.

As was to be expected, the maintenance of rebound contraction was not as long under these conditions as in the intact animal, but with both myotatic and tonic labyrinthine reflexes eliminated, we observed

6. Bechterew, V.: Die Funktionen der Nervencentra, Jena, Gustav Fischer, 1909, vol. 2, p. 919.

7. Bremer, F.: Contribution à l'étude de la physiologie du cervelet: La fonction inhibitrice du paléo-cérébellum, Arch. internat. de physiol. **19**:189, 1922.

8. Miller, F. R., and Laughton, N. B.: Myograms Yielded by Faradic Stimulation of the Cerebellar Nuclei, Proc. Roy. Soc., London, s.B **103**:575 (Nov. 1) 1928.

9. Denny-Brown, D.; Eccles, J. C., and Liddell, E. G. T.: Observations on Electrical Stimulation of the Cerebellar Cortex, Proc. Roy. Soc., London, s.B **104**:518 (May 4) 1929.

astounding periods of continued discharge following cessation of cerebellar stimulation, many of the rebounds persisting for a minute or longer. These observations have led us to the view that under these conditions the prolonged discharge of efferent centers which underlies the maintenance of these contractions belongs in the category of nervous activity described as after-discharge in the case of monophasic responses.

This prolonged discharge differs from the after-discharge of monophasic responses in that it is not a direct continuation of the effect manifest during stimulation. If the electrical stimulation activates the mechanism responsible for the rebound, as it must do, this activity is not overtly expressed until stimulation has ceased, when, in the absence of the effect occurring during stimulation, the rebound activity manifests itself in the posture of the animal and is continued far beyond a length of time for which the brief influence of a short stimulation could be directly responsible. Some process of continued central excitement must be active in these prolonged rebound effects, and in explanation of just such activity the hypothesis of closed, reverberating, or self-reexciting neuron circuits has been advanced by one of us (S. W. R.) and Hinsey [10] and by Lorente de Nó.[11]

The appearance of these reactions, caused by cerebellar stimulation in the deafferented animal, does not differ from that in the normal animal. The response consists of a rebound flexion and adduction of the right forelimb appearing after cessation of stimulation of the left side of the cerebellum. The rebound posture is marked and rigid and strongly resists passive manipulation. It is persistent, although not as long lasting as in the normal animal.

A rebound extension of the deafferented right forelimb follows cessation of stimulation of the right side of the cerebellum. The extensor contraction is marked—equal, for example, to a high grade of decerebrate rigidity. When at or near its maximum, it will easily support the weight of the body. The posture is maintained for a considerable period, although not for as long as in the normal animal.

The localization of the points at which stimulation yielded the reactions obtained from this series of animals is shown in figure 1, in six horizontal sections through the interior of the cerebellum. The circles represent the localization of the points at which stimulation was followed by a rebound extension of the deafferented right forelimb, and

10. Ranson, S. W., and Hinsey, J. C.: Reflexes in the Hind Limbs of Cats After Transection of the Spinal Cord at Various Levels, Am. J. Physiol. **94**:471, 1930.

11. Lorente de Nó, R.: Researches on Labyrinth Reflexes, Tr. Am. Otol. Soc. **22**:287, 1932; Vestibulo-Ocular Reflex Arc, Arch. Neurol. & Psychiat. **30**:245 (Aug.) 1933; Studies on the Structure of the Cerebral Cortex, J. f. Psychol. u. Neurol. **45**:381, 1934; Facilitation of Motoneurones, Am. J. Physiol. **113**:505, 1935.

these points are all seen to be on the right, or ipsilateral, side of the cerebellum. The crosses indicate the localization of points at which stimulation was followed by a rebound flexion of the deafferented right forelimb, and such points are all seen to be located on the left, or contralateral, side of the cerebellum. It is clear that these reactions have been obtained from stimulation of the underlying folia of the cerebellar cortex of the vermis, both of the anterior lobe and of more posteriorly lying parts. These reactions may be followed ventrally through the underlying white matter to the region of the medial cerebellar nuclei, and many responses have been obtained from stimulation of points in the medial nuclei themselves. This localization does not differ from that found in the normal animal.[2]

Figure 2 illustrates the number of rebound contractions obtained from this series of deafferented animals, indicated by intervals along the abscissas, together with the length of time for which these contractions were maintained, shown in seconds along the ordinates. The series has been separated into two groups, of seven and six animals, respectively, depending on whether the labyrinths were intact or had been removed. The other operative procedures were identical in the two groups. Figure 2 *A* and *B* illustrate rebound extension (*A*) and rebound flexion (*B*) in deafferented limbs in animals in which the labyrinths were intact. Figure 2 *C* and *D* illustrate rebound extension (*C*) and rebound flexion (*D*) in deafferented limbs in animals in which the labyrinths had been removed.

The first, and most important, thing which can be observed from the data shown in figure 2 is the duration of the tonic after-discharge in the absence of tonogenic afferent impulses. Flexor contractions are seen persisting for varying periods up to as high as sixty (fig. 2 *B*) or sixty-five seconds (fig. 2 *D*). Extensor contractions are seen persisting for periods ranging up to ninety (fig. 2 *C*) and ninety-five seconds (fig. 2 *A*). There appears to be a tendency, seen in both groups, for extensor discharge to outlast flexor discharge, as indicated by the existence of more extensor than flexor rebounds in the upper brackets of duration.

Holding the neck concave to one side or the other during the course of these experiments did not affect the duration of the rebound contractions in twelve instances, while in three instances concavity of the neck to the contralateral side slightly favored the extensor posture of the deafferented forelimb. We readily admit the possibility that when the animals are in the usual hanging position, the dorsiflexion of the neck might favor the duration of extensor rebounds, but it should be noted that this position did not prevent the occurrence of prolonged flexor rebounds, although it should be directly antagonistic to them.

The duration of rebound contraction in the right forelimb did not differ materially in animals in which the opposite, or left, forelimb had been denervated from that in which the left forelimb retained its nerve supply. The effect of cutting the spinal cord was variable and will be discussed shortly.

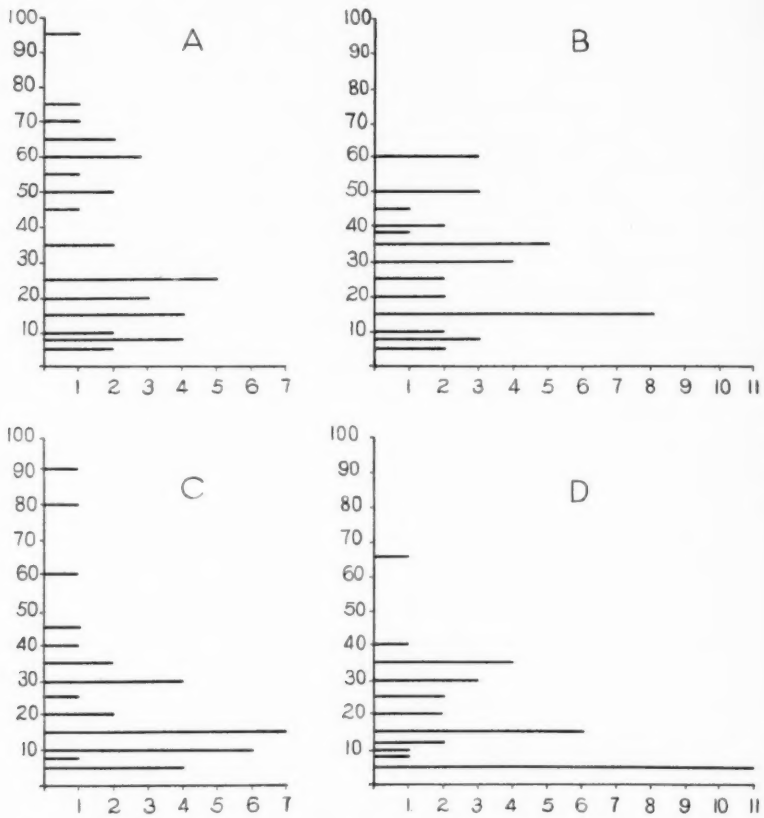

Fig. 2.—Chart showing the number of rebound contractions obtained from the series of deafferented animals (indicated on the abscissas) and the length of time, expressed in seconds, for which these contractions were maintained (indicated on the ordinates). The series has been separated into two groups: *A* and *B* showing rebound extension (*A*) and rebound flexion (*B*) after deafferentation alone, and *C* and *D* showing rebound extension (*C*) and rebound flexion (*D*) after labyrinthectomy in addition to deafferentation. The total of 138 responses is distributed as follows: *A*, 34; *B*, 38; *C*, 32, and *D*, 34. The right forelimb, in which the duration of these contractions was observed, was deafferented in all 138 responses. The left forelimb was denervated in 10 responses, in *A;* in 24, in *B;* in 32, in *C*, and in 34, in *D*. The lower thoracic portion of the cord was sectioned in 6 responses, in *A;* in 14, in *B;* in 9, in *C*, and in 10, in *D*. The labyrinths were removed in all 67 responses, in *C* and *D*.

Elimination of the afferent nerves from the reacting limb (fig. 2 *A* and *B*) appears to cut down the duration of rebound contraction by a rather long period, if one takes several minutes to be the duration of these contractions in the normal animal. Removal of the labyrinths in addition to deafferentation seems to shorten this duration a little more, for there appears to be a tendency for both extensor and flexor rebounds to be reduced slightly more after labyrinthectomy than after deafferentation alone. This is indicated by the presence of a large number of responses in the lower brackets of duration after labyrinthectomy (fig. 2 *C* and *D*).

The possibility that this decreased duration of rebound contraction may be due to a weakened condition of the animal, as a result of the severe preliminary operations, is not excluded, but it is probable that reflexes occasioned by afferent impulses from the limbs and labyrinths are able to append themselves to and prolong the maintenance of rebound discharge following cerebellar stimulation. It is clear, however, that this discharge is independent of such reflexes, for in their absence it is still present for durations up to a minute or longer. In other words, this prolonged discharge of efferent neurons may still be obtained after the elimination of all the afferent impulses on which the tonic effects of the stretch and labyrinthine reflexes depend.

In all the responses which have just been considered, the reacting limb was flaccid before cerebellar stimulation, and the rebound contraction which followed cessation of stimulation gradually decreased until the tone of the limb had again disappeared. This disappearance of tone is an essential criterion for considering these effects as representing an uncomplicated type of after-discharge, for it is known that another, more persistent, tonic contraction may occur as a release phenomenon following cerebellar destruction.

Effects of Cerebellar Release.—Evidences of these release effects were first encountered by us in experiments on the normal animal, when after excessive puncturing and stimulation of one side of the medial portion of the interior of the cerebellum, persistent extensor rigidity of the ipsilateral forelimb was found to have developed imperceptibly from successive rebound extensor contractions. This persistent extensor rigidity could still be completely inhibited during the period of cerebellar stimulation, but it reappeared in full strength in the rebound. It differed, however, from the normal rebound not only in persisting indefinitely but in the respect that subsequent stimulation on the opposite side of the cerebellum was no longer able to reverse the posture to one of rebound flexion, as in the case of uncomplicated responses. After such persistent extensor rigidity of one forelimb had developed, stimulation on

the contralateral side of the cerebellum could still inhibit the contraction, but the extensor rigidity either immediately reappeared in the rebound or quickly overcame the transient rebound flexion of the limb which sometimes occurred.

These release effects constitute an important problem, both in themselves and in their relation to the rebound contractions normally following cessation of cerebellar stimulation. For this reason, a number of experiments have been performed which were concerned, first, with the production of such effects by different means and, second, with the demonstration that they are not irritative phenomena but truly release effects.

The production of extensor rigidity of both forelimbs by complete extirpation of the cerebellum was verified in four normal animals, in only one of which was any information presented additional to that established by other investigators. In this animal, prolonged extension of the right forelimb and flexion of the left forelimb were first obtained as a rebound after cessation of stimulation of the right side of the cerebellum. The cerebellum was then quickly removed in the initial phase of a rebound, and the rebound posture was found to be succeeded immediately by extensor rigidity identical in both forelimbs. This phenomenon of cerebellar release is not new. Clearcut evidence of extensor hypertonus due to release from cerebellar inhibition has been furnished by Bremer [3] and by Pollock and Davis.[12] The anemic method of cerebellar destruction employed by Pollock and Davis has ruled out the possibility of irritation as a causative factor, and the experiments now to be reported serve to confirm their observations in other ways.

In five normal animals the interior of one side of the medial portion of the cerebellum was systematically riddled with electrode punctures, without electrical stimulation. Before puncturing was begun, the tone was slight and its distribution symmetrical on the two sides of the body. In all five animals repeated puncturing led to the development of extensor tone in the ipsilateral forelimb. This was transient in one case but persisted indefinitely in the other four animals. Development of transient extensor tone in the ipsilateral hindlimb occurred in two animals. Transient flexor tone in the contralateral forelimb and hindlimb developed in one animal. The head became turned to the contralateral side in two animals. In the three animals in which it was performed, subsequent damage by repeated puncturing of the opposite side of the cerebellum led to the development of extensor tone in the

12. Pollock, L. J., and Davis, L.: The Influence of the Cerebellum upon the Reflex Activities of the Decerebrate Animal, Brain **50**:277, 1927; The Reflex Activities of a Decerebrate Animal, J. Comp. Neurol. **50**:377, 1930.

forelimb on that side, both forelimbs then remaining extended indefinitely.

The efferent connections from this region were eliminated by undercutting the medial portion of the interior of the cerebellum in three normal animals in a horizontal plane passing just under the medial cerebellar nuclei and severing their descending connections on either side. In all three animals such a section led to marked and persistent extensor rigidity of both forelimbs, and in one case, to a slight gain in extensor tone in both hindlimbs. One of these animals showed pronounced dorsiflexion of the neck and increased extensor tone in the forelimbs when on its side or back. The other animals were not examined in these positions.

In an effort to rule out all mechanical destruction, with its possible consequent irritation of cut or injured surfaces, these release effects were produced by narcosis of the intact cerebellum through the injection of a solution of cocaine into its interior. In two normal animals injection of a 0.5 per cent solution of cocaine hydrochloride into the medial portion of one side of the interior of the cerebellum was followed by strong extensor rigidity of the ipsilateral forelimb. Subsequent injection into the opposite side of the cerebellum led to extensor rigidity of the forelimb on that side, both forelimbs then remaining extended indefinitely. The one animal which was so examined also exhibited pronounced dorsiflexion of the neck when on its side or back. In a third normal animal injection of an 8 per cent solution of cocaine hydrochloride into one side of the medial portion of the interior of the cerebellum produced rigid extension of both forelimbs, which persisted until the animal died five minutes later, of respiratory failure, due, undoubtedly, to spread of cocaine to the medulla.

Since the question of the identity of cerebellar release effects and the rebound activity following cessation of cerebellar stimulation has been raised (Miller and Laughton [8]), it may be pointed out, in the light of the observations just presented, that in several respects the two do not appear to be homologous. First, cerebellar release effects are prolonged indefinitely. Second, when these effects are released from one side of the cerebellum, they cannot be reversed in the rebound following cessation of stimulation of the opposite side of the cerebellum. Third, the posture of release due to destruction of one side of the cerebellum does not appear to be identical with the rebound posture induced from that side of the cerebellum. The only consistent release effect which we have observed from one side of the cerebellum is extension of the ipsilateral forelimb, which falls far short of duplicating a typical rebound posture, which includes also flexion of the contralateral foreleg and usually some participation of the hindlimbs and the body axis. Descriptions by other workers of release effects following hemi-

decerebellation in the chronic animal (Dusser de Barenne,[13] Rademaker[14] and Obrador Alcalde[15]) reveal actual discrepancies between the two, in that the concavity of the body axis is toward the injured side after hemidecerebellation while it is toward the contralateral side in the rebound following stimulation of one half of the cerebellum.

Effect of Section of the Spinal Cord.—In six of the thirteen deafferented animals, phenomena were encountered subsequent to cerebellar stimulation which simulated in some particulars the release effects just described for the normal animal. In these instances extensor rebound was prolonged into more or less persistent extensor rigidity, lasting, in the deafferented forelimb, for from nine minutes to over three hours. The effect was independent of the innervation of the other limbs or of the labyrinths, for it occurred in animals in which this innervation had been eliminated.

The persistent extensor posture could be completely inhibited during cerebellar stimulation, but it immediately returned, sometimes in augmented strength, in the rebound. It could not be reversed in the rebound following stimulation of the opposite side of the cerebellum. In the latter case, the limb either rebounded immediately into extension or exhibited a short-lasting rebound flexion, which soon passed once more into extensor rigidity.

In five of these animals some factor associated with cutting the spinal cord appeared to have been responsible for the prolonged duration of the nervous activity set into play in the rebound following cessation of cerebellar stimulation. In two animals the effect was well controlled, in that stimulation prior to section of the cord was performed at points on the first and second insertions of the electrodes into the cerebellum, the rebounds following stimulation of these points persisting for twenty-five and thirty seconds, respectively, and the limbs then becoming flaccid. Section of the spinal cord produced some extensor tone in the deafferented forelimb, and the marked rebound extension following stimulation of these same points shortly after section of the cord became persistent extensor rigidity, enduring for more than nine minutes in one animal and, with variations in intensity, for over three hours in the other. In three other animals similar, but less clearcut, effects were obtained.

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13. Dusser de Barenne, J. G.: Die Funktionen des Kleinhirns, in Alexander, G., and Marburg, O.: Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1923, vol. 1, p. 589.

14. Rademaker, G. G. J.: Das Stehen, in Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1931, no. 59, p. 364.

15. Obrador Alcalde, S.: Algunos reflejos posturales y muskulares en perros privados del cerebelo, Arch. de neurobiol. **14**:537, 1934.

This augmentation of activity of the extensor centers of the forelimb after section of the lower thoracic portion of the spinal cord appears similar in principle to the augmentation of extensor reflexes in the forelimb following postbrachial section of the spinal cord in the experiments of Ruch,[16] Miller,[17] Ruch and Watts [18] and Ruch [19] and suggests the possibility that one may be dealing here with the same effect (Schiff-Sherrington phenomenon).

In seven animals of the deafferented series, no grossly observable effect on rebound contraction of cutting the spinal cord could be noted; in four of these animals the cord was cut when the electrodes were at a point yielding rebound extension, and in three, when at a point yielding rebound flexion after cerebellar stimulation.

Effect of Ephedrine.—In one animal of the series, in which the rebound contraction of the deafferented forelimb relaxed after a maximum duration of thirty-five seconds and in which section of the spinal cord had had no apparent effect, intravenous injection of ephedrine hydrochloride (Hinsey, Ranson and Zeiss [20] and Jacobsen and Kennard [21]) was tried toward the end of the experiment. This, in itself, produced no tone in the deafferented limb, but subsequent rebound extension, following stimulation at the same point as before injection, became persistent extensor rigidity, lasting for at least a half-hour. In this animal, also, the opposite forelimb had been denervated and the labyrinths removed.

Effect of Painful Stimulation.—In the animals of the deafferented series, painful stimulation of innervated parts of the body augmented or even reproduced the rebound contractions following cessation of cerebellar stimulation, once these rebounds had occurred. The best effects were obtained from pinching the ear, the tongue or the conjunctiva (fifth nerve); pinching the thoracic wall (lower intercostal nerves) produced the same effect, but to a less marked degree. In

16. Ruch, T. C.: Release of Extensor Rigidity of the Forelimb by Separation from Lumbosacral Segments, J. Physiol. **76**:3P, 1932.

17. Miller, F. R.: Reflexes in the Triceps Extensor Preparation of the Forelimb, J. Physiol. **81**:194, 1934.

18. Ruch, T. C., and Watts, J. W.: Reciprocal Changes in the Reflex Activity of the Forelimbs Induced by Post-Brachial "Cold-Block" of the Spinal Cord, Am. J. Physiol. **110**:362, 1934.

19. Ruch, T. C.: Evidence of the Non-Segmental Character of Spinal Reflexes from an Analysis of the Cephalad Effects of Spinal Transection (Schiff-Sherrington Phenomenon), Am. J. Physiol. **114**:457, 1936.

20. Hinsey, J. C.; Ranson, S. W., and Zeiss, F. R.: Observations on Reflex Activity and Tonicity in Acute Decapitate Preparations, With and Without Ephedrine, J. Comp. Neurol. **53**:401, 1931.

21. Jacobsen, C. F., and Kennard, M. A.: The Influence of Ephedrine Sulphate on the Reflexes of Spinal Monkeys, J. Pharmacol. & Exper. Therap. **49**:362, 1933.

six of the instances now to be reported, the effect definitely outlasted the period of painful stimulation.

In three of the animals just described, in which the spinal cord had been divided and persistent extensor tone developed after cessation of cerebellar stimulation, painful stimulation reenforced this extensor tone in four instances, inhibited it in one instance and caused alternating flexion and extension in one instance. In five other animals painful stimulation after a rebound extensor contraction had subsided produced extension of the limb in eight instances. Painful stimulation after a rebound flexor contraction had subsided produced flexion of the limb in three instances and stepping in one instance. In one animal pinching the ear after a rebound flexion had subsided led in three instances to a biphasic response. The effect during stimulation was mixed, the limb being flexed and occasionally or rhythmically extended. Immediately pinching was stopped, the limb was extended. Painful stimulation before cerebellar stimulation was begun produced either an occasional, inconstant movement of the deafferented limb or no effect in this limb.

In four animals of the deafferented series, seven responses were encountered in which, after varying intervals following cerebellar stimulation, the resulting rebound extension was interrupted by a periodic brief inhibition, followed by a strong return of extensor tone, the sequence of events resembling a rhythmic stepping. There is no reason to believe, however, that painful stimulation was the cause of these effects.

None of the responses described in the three preceding sections has been included in the data shown in figure 2.

SUMMARY

The prolonged maintenance of rebound excitation following cerebellar stimulation in the normal animal is considerably reduced by deafferentation of the reacting limb and appears to be decreased a little more by labyrinthectomy in addition to deafferentation. After the elimination, however, of all the afferent impulses on which the tonic effects of the stretch and labyrinthine reflexes depend, continued discharge of both flexor and extensor centers for the forelimb has been observed for periods of up to a minute or longer.

Release effects have been produced by destruction of the cerebellum in several ways and have been compared with the rebound contractions which follow the cessation of cerebellar stimulation. In a number of respects the two do not appear to be homologous.

AGENESIS OF THE CORPUS CALLOSUM

ITS RECOGNITION BY VENTRICULOGRAPHY

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Agenesis of the corpus callosum, both partial and complete, has been reported repeatedly as an unexpected autopsy observation. The five cases described in this communication are the first to be recognized during life, but the ventriculograms when once seen and understood could scarcely be mistaken for those showing any other condition. It is anticipated, therefore, that when clinicians generally recognize the ventriculographic features of these cases, the condition may be found to be less rare than is supposed and further knowledge of the function of the corpus callosum may be forthcoming.

Up to the year 1933, Baker and Graves [1] could find only eighty-two cases of this condition reported in the medical literature, although the first example was described as long ago as 1812, by Reil.[2] A brief analysis of the normal and abnormal development of the corpus callosum and a discussion of published views on its function are added herewith to a description of the cases of five living patients. Further outline is given of the ventriculographic features which make it possible to recognize the condition and to distinguish complete from incomplete agenesis of this great commissure.

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The words pathologic and neurologic are used in this article only in order to conform to the terminology which is compulsory for publication in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. We should prefer to use the words pathological and neurological.

This paper was read by title at the Sixtieth Annual Meeting of the American Neurological Association in June 1934, after which it appeared in summary form in the *Transactions of the American Neurological Association* (**60**:182, 1934). At the same meeting an excellent article on this subject by Davidoff and Dyke also was read by title and has since been published in full (Agenesis of the Corpus Callosum: Its Diagnosis by Encephalography; Report of Three Cases, Am. J. Roentgenol. **32**:1 [July] 1934).

1. Baker, R., and Graves, G.: Partial Agenesis of the Corpus Callosum, Arch. Neurol. & Psychiat. **29**:1054 (May) 1933.

2. Reil, J.: Mangel des mittleren und freien Theils des Balkens im Menschengehirn, Arch. f. d. Physiol. **11**:341, 1812.

ANALYSIS OF THE LITERATURE

(*a*) *Embryology of the Corpus Callosum.*—In the 3.2 mm. human embryo the neural tube has closed except for the anterior and posterior neuropores.[3] At this stage the future ventricular system is a single cavity. From this stage on, however, the pallium of the telencephalon expands bilaterally and thus begins the bilateral reduplication of the ventricles. The lamina between the two hemispheres remains stationary, making possible the longitudinal fissure which comes to be occupied by the falx.

The first evidence of development of the corpus callosum in the human fetus is seen in the third month as a thickening on the lamina terminalis (fig. 1 *A*). The corpus callosum makes its appearance grossly along with and contiguous to the hippocampal commissure of the fornices (fig. 1 *B*). These two structures then grow rapidly and extend posteriorly over the fimbria and thalamus (fig. 1 *C* to *E*).

The most anterior aspect of the corpus callosum develops first and is situated on the lamina terminalis. In progressing posteriorly, its splenium normally being in contact with the hippocampal commissure, it carries beneath it the septum pellucidum, the triangular structure which comes to be bounded by the hippocampal commissure of the fornices posteriorly, the corpus callosum superiorly and anteriorly and the lamina rostralis inferiorly. The development is not complete until the fifth month. It can be seen that the development of the corpus callosum, of the hippocampal commissure and of the septum pellucidum go hand in hand.

On an embryologic basis, therefore, if complete or partial absence of the corpus callosum occurs as the result of arrested development, one might expect that other associated structures would fall short of complete evolution.

(*b*) *Suggested Causes of Agenesis.*—The causes usually advanced to explain developmental anomalies in general have been suggested in this instance. Inflammation (ependymitis), syphilis and chemical toxins have been proposed, though with no substantial evidence. Internal hydrocephalus has received the most consideration, obviously because the defect is often associated with some degree of hydrocephalus. De Lange[4] suggested that hydrocephalus may prevent the development of the corpus callosum by separating the two hemispheres. Cameron[5]

3. Keibel, F., and Mall, F.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910, vol. 2, p. 35.

4. de Lange, C.: On Brains with Total and Partial Lack of the Corpus Callosum and on the Nature of the Longitudinal Callosal Bundle, J. Nerv. & Ment. Dis. **62**:449, 1925.

5. Cameron, J. L.: The Corpus Callosum: A Morphological and Clinical Study, Canad. M. A. J. **7**:609 (July) 1917.

stated the belief that the hydrocephalus is a result and is more apparent than real, since the corpus callosum normally forms the roof of the lateral ventricles. At any rate, hydrocephalus, except for the practically constant dilatation of the posterior horns, is not always present. In any case, it seems inconceivable that hydrocephalus could precede the formation of the corpus callosum.

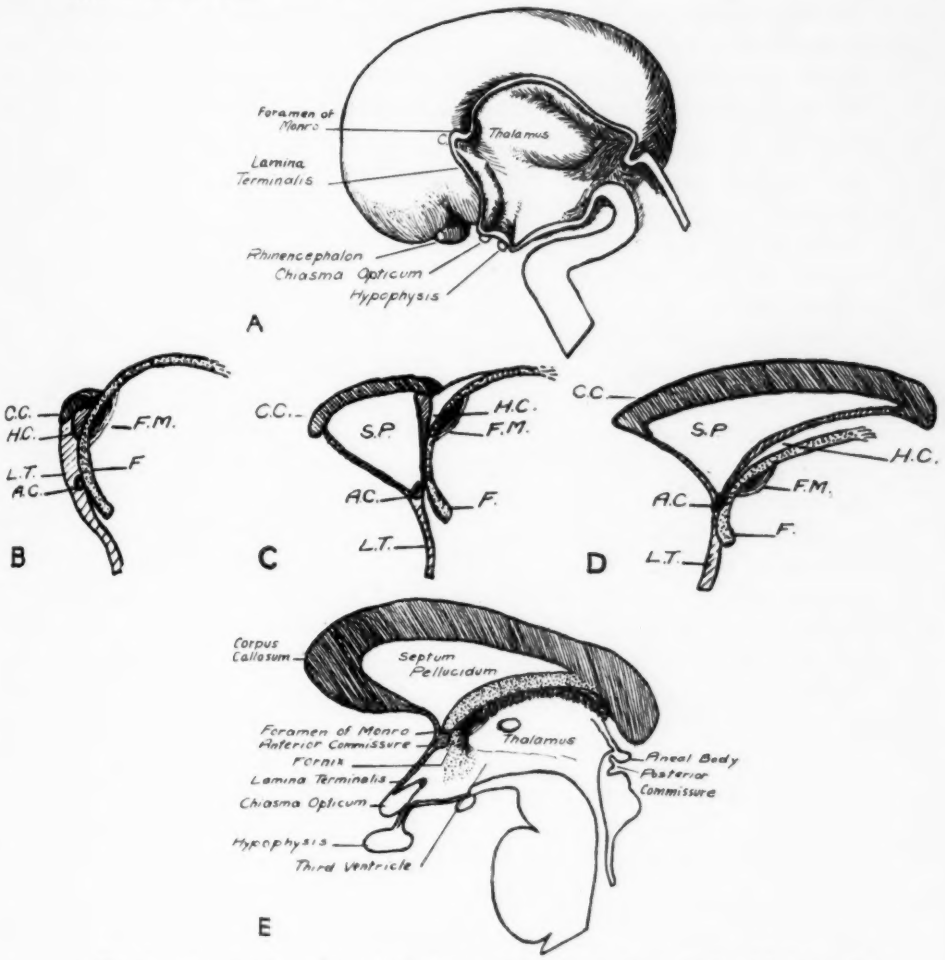

Fig. 1.—*A*, mesial section of the brain of a human fetus in the third month. *C* indicates thickening of the lamina terminalis, which normally develops into the corpus callosum. *B*, a schematic representation of the structures in a human fetus at the third month. *C.C.* indicates corpus callosum; *H.C.*, hippocampal commissure; *L.T.*, lamina terminalis; *A.C.*, anterior commissure; *F.M.*, foramen of Monro, and *F.*, fornix. *C*, the corpus callosum at four months. *S.P.* indicates septum pellucidum. *D*, the corpus callosum at the fifth month. *E*, a diagrammatic representation of a mesial section of the normal corpus callosum of an adult human being and its related structures.

Several cases of agenesis of the corpus callosum associated with lipoma have been reported. Huddleson [6] reported one case in which a lipoma was situated between the frontal lobes. Huebschmann [7] reported a case of partial absence, with a lipoma situated on the genu of the corpus callosum. This association with lipoma is seen also with another type of developmental anomaly—spina bifida. De Lange [4] pointed out that the anterior commissure is abnormally well developed in some cases of agenesis, but it is difficult to consider arrested development of the corpus callosum as a reversion to primitive type, because the rhinencephalon itself suffers in the cases of most complete agenesis.

Whatever the cause may eventually prove to be, one is obviously dealing with cases of arrest of the normal development of the callosal body, which may occur at any stage.

(*c*) *Comparative Anatomy.*—Absence of the corpus callosum in animals has been reported. Tumbelaka [8] has described total absence in a cebus monkey, and King and Keeler [9] have made an interesting report of the absence of the corpus callosum in a strain of house mice, many of the members of which presented also an abnormal absence of rods in the retina. These authors stated the opinion that the anomaly of the corpus callosum is undoubtedly not due to the presence of the rodless gene. They showed that in mice the agenesis is definitely familial in occurrence and probably inherited as a unit character. It segregates sharply, the corpus callosum being either present or entirely absent in the animals studied. There is no evidence of sex linkage. By superficial examination the reactions of mice with and without a corpus callosum could not be distinguished.

(*d*) *Pathologic Anatomy.*—One of the earliest stages of arrested development with the cranium intact is illustrated by a case described by Turner.[10] This was the case of a man aged 48 who, because he was subject to severe epileptic seizures, had been admitted to a hospital for patients with mental disease at the age of 23. The essential facts in the description of the brain in this case are as follows: The hemispheres were joined together by mesial convolutions and not divided in the

6. Huddleson, J.: Ein Fall von Balkenmangel mit Lipomentwicklung im Defekt, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:177, 1928.

7. Huebschmann: Ueber einige seltene Hirntumoren: III. Lipom des Balkens bei partiellem Balkenmangel, Deutsche Ztschr. f. Nervenh. **72**:222, 1921.

8. Tumbelaka, R.: Das Gehirn eines Affen worin die interhemisphäriale Balkenverbindung fehlt, Folia neuro-biol. **9**:1, 1915.

9. King, Lester S., and Keeler, Clyde E.: Absence of Corpus Callosum: A Hereditary Brain Anomaly of the House Mouse; Preliminary Report, Proc. Nat. Acad. Sc. **18**:525, 1932.

10. Turner, W.: A Human Cerebrum Imperfectly Divided into Two Hemispheres, J. Anat. & Physiol. **12**:241, 1878.

normal manner. The falx and the great longitudinal fissure were absent. There was a single large ventricle in the midline, without lateral horns. The corpus callosum, fornices, septum pellucidum, velum interpositum and choroid plexuses were reported to be absent. Turner stated that the only other case recorded which resembles his was one referred to by Mihalkovics, which was supposed to have been described by Bianchi. Though Turner did not see the original description, he gave the following reference: "Storica del monstro di duc corpi, Turino, 1749, p 100." In this case the hemispheres were grown together in the mesial plane, and the ventricular system was one common cavity.

A later stage of arrested development is illustrated by the case of Hinrichs,[11] in which the anterior three quarters of the cerebrum was not separated completely into halves. The corpus callosum, fornices, septum pellucidum and olfactory bulbs were absent. Hinrichs explained the maldevelopment of the forebrain by the absence of the olfactory bulbs, but it is difficult to distinguish cause from effect here. The ventricle was a single cavity in this instance also, with only slight indentation of its roof by the longitudinal fissure posteriorly.

Segal[12] has recently reported two cases of complete absence and one case of deformity of the commissure, recognized post mortem. In one of these cases no rhinencephalic structures were present. The olfactory bulbs, olfactory tracts, fimbria and fornices were absent.

Complete absence of the corpus callosum has been found in a little more than half of all the cases reported. In these cases the septum pellucidum is always absent. The fornices are usually visible but are often separated as a result of a poorly developed or absent hippocampal commissure, allowing the third ventricle to be in free communication with the space anterior to the fornices. Hydrocephalus may be present to a varying degree, but enlargement of the posterior horns is a practically constant feature.

Other congenital defects are often associated with complete agenesis, such as microcephaly, porencephaly and polygyria, the type of cortical configuration tending to be fetal. Associated defects are at times present and remote from the central nervous system. Cameron[13] reported the case of a girl aged 15 years with absence of the corpus callosum and with the stomach completely in the right side of the chest.

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11. Hinrichs, U.: Ueber eine durch Balken- und Fornixmangel ausgezeichnete Gehirnmissbildung, Arch. f. Psychiat. **89**:57, 1929.

12. Segal, M.: Agenesis of the Corpus Callosum in Man, South African J. M. Sc. **1**:65 (Sept.) 1935.

13. Cameron, J., and Nicholls, A.: Two Rare Abnormalities Occurring in the Same Subject: Partial Absence of the Corpus Callosum; the Stomach Situated Entirely Within the Thorax, Canad. M. A. J. **11**:448, 1921.

Partial absence of the corpus callosum varies all the way from development of only a rudimentary bundle of fibers in the region of the genu, and hence absence of the septum pellucidum, as in the case of Cameron, to a corpus callosum which is practically complete except for a defect in the region of the splenium.

Bruce [14] divided defects of the corpus callosum into four main types according to the embryonic period in which arrest takes place: 1. If arrest occurs during the first three weeks of embryonic life, the cerebrum will consist of a single vesicle and the ventricle of a single cavity. The corpus callosum, septum pellucidum, fornices, velum interpositum and anterior commissure will be absent. 2. If arrest occurs before the fourth month, the hemispheres will be divided, but the corpus callosum, septum pellucidum, lyra of the fornices and anterior commissure will be absent. 3. If development continues until the fourth month, the laminae of the septum pellucidum will join at their anterior inferior angles, forming the anterior commissure. 4. If arrest occurs at about the end of the fourth month, the genu of the corpus callosum will be present, plus an extension posteriorly, depending on the degree of union of the marginal arches.

(*c*) *Structure and Supposed Function of the Corpus Callosum.*—The late ontogenetic development of the corpus callosum is in conformity with the fact that phylogenetically speaking it is the most recently developed of the three commissures of the forebrain. Its presence exclusively in higher mammals provides zoologists with a means of dividing this highest class of vertebrates into two distinct subclasses—the callosal and the acallosal mammals. In the lowest group of callosal mammals (Edentata) it is little more than a membranous structure. It is comparatively thin in the rabbit and reaches its highest degree of development in the primates. The formation of convolutions in the human brain increases the total volume of gray matter threefold, and the size of the corpus callosum is always proportional to this volume.[5]

Mingazzini, quoted by Armitage and Meagher,[15] has demonstrated the origin of some of the callosal fibers from pyramidal cells in the cortex. Hamilton [16] as early as 1885 showed that some of the fibers after crossing in the corpus callosum end in identical and distant areas of the cortex, while others become lost in the thalamus and in the internal and external capsules.

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14. Bruce, A.: On the Absence of the Corpus Callosum in the Human Brain, with the Description of a New Case, Brain **12**:171, 1889.

15. Armitage, G., and Meagher, R.: Gliomas of the Corpus Callosum, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:454, 1933.

16. Hamilton, D.: On the Corpus Callosum in the Adult Human Brain, J. Anat. & Physiol. **19**:385, 1885.

The presence of motor projection pathways in the corpus callosum is demonstrable by electrical stimulation, according to Mott and Schaefer.[17] Movements of the head and neck are apparently provoked by stimulation of the genu, and toward the splenium the motor response progresses caudad. The splenium seems to be devoid of motor components.

Of the clinical manifestations which have been associated with partial or complete absence of the corpus callosum, feeblemindedness and epilepsy are the most frequent. Feeblemindedness has varied in degree from idiocy, with the ability to utter only unintelligible sounds, to only a slight departure from normal. The epileptic seizures have been typical of petit mal or grand mal. Other clinical findings have been spastic paraplegia, nystagmoid movements of the eyes and continued movements of the hands, as in piano playing.[4] Cameron claimed that defects other than those of the corpus callosum have accounted for spastic paraplegia and epileptic seizures in these cases, and he advanced the opinion that the great commissure is of importance in governing only the finer coordinations and not in regulating the higher function of mentality. He stated the opinion that it is clear that total absence is possible without any pathognomonic alteration in the subject's physical or mental capacity.

The proof of such a contention would have to be based on the existence of a case or cases in which there was proved complete absence of the corpus callosum in a patient who, during life, presented no clinical abnormality. In all the cases reported in the literature it has been necessary for the author to study the patient's life in retrospect, after the postmortem examination had revealed the diagnosis. In a number of cases the patient has been reported in this way to have been normal, notably in five cases collected by Bruce.[14] He concluded from a study of fifteen cases reported in the literature and one of his own that if the brain is otherwise well developed, absence of the corpus callosum does not necessarily produce any disturbance of motility, coordination, general or special sensibility, reflexes, speech or intelligence.

It has been considered by some clinicians that the corpus callosum has to do with eupraxia. In conformity with this point of view, Critchley,[18] in discussing the results of occlusion of the anterior cerebral artery, attributed ideomotor apraxia to destruction of the anterior portion of the corpus callosum. Positive deductions from the study of patients presenting gross lesions of the corpus callosum may be easily

17. Mott, F., and Schaefer, E.: On Movements Resulting from Faradic Excitation of the Corpus Callosum in Monkeys, Brain **13**:174, 1890.

18. Critchley, M.: The Anterior Cerebral Artery and Its Syndromes, Brain **53**:120, 1930.

misleading because of the inevitable involvement of important neighborhood structures. This is especially true of cases of tumor of the brain, as was pointed out by Armitage and Meagher,[15] who could assign no function to the corpus callosum after an exhaustive study of cases in Cushing's clinic. Further, these authors could detect no apraxia in patients after partial section of the corpus callosum in the midline and found no evidence of disturbance in motor or mental reactions in Macacus rhesus monkeys after complete transection of the commissure.

Dandy[19] stated that he has occasionally found it necessary in operative procedures to divide the corpus callosum in its entire anteroposterior extent and has noted no unusual results. Hartmann and Trendelenburg,[20] using both rhesus and Javanese monkeys, taught the animals to perform a complicated series of bimanual movements requiring the simultaneous use of both hands in obtaining food. After total section of the callosum these animals showed not the slightest evidence of apraxia.

Such negative reports may rectify false conclusions, but they leave unanswered the question of what may be the function of this large structure. The experiments of Pavlov[21] are more constructive. He found that if a reflex is conditioned on one side of the body (i. e., a tactile-salivary reflex), then tactile stimuli applied to corresponding locations on the opposite side of the body evoke the same reflex. The same marked specificity was maintained for areas of the skin on the two sides of the body, and the same result was obtained with the use of excitatory or inhibitory reflexes. When the corpus callosum was divided by operation, the phenomenon was entirely abolished. That is to say, it was necessary to condition the reflex on the two sides of the body independently in order to establish them. This suggests that the afferent pathway from the peripheral receptor to its representation in the opposite hemisphere branches to reach an area of homologous representation in the ipsilateral hemisphere by way of the corpus callosum.

REPORT OF CASES

CASE 1.—N. McK., a girl aged 8 years, was referred by Dr. Alton Goldbloom, of Montreal, Canada, in March 1932, with the complaint of jacksonian convulsions.

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19. Dandy, W. E.: Congenital Cerebral Cysts of the Cavum Septi Pellucidi (Fifth Ventricle) and Cavum Vergae (Sixth Ventricle), Arch. Neurol. & Psychiat. **25**:44 (Jan.) 1931.

20. Hartmann, F., Jr., and Trendelenburg, W.: Zur Frage der Bewegungsstörungen nach Balkendurchtrennung an der Katze und am Affen, Ztschr. f. d. ges. exper. Med. **54**:578, 1927.

21. Pavlov, I.: Conditioned Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex, translated and edited by G. Anrep, London, Oxford University Press, 1926.

The mother's pregnancy had run a normal course, except for the removal of an ovarian cyst during the third month. The infant was delivered at full term with forceps after a forty-eight hour labor. There were superficial bruises and a slight internal squint, which persisted, but there was no evidence of injury of the brain, as the child seemed normal otherwise. She nursed well and walked and talked at the usual ages. She became left handed, and no attempt at correction was made.

At the time of her first admission to the hospital she was in the second grade at school and doing well in all subjects, being poorest in mathematics. She played normally, showing no evidence of backwardness or introversion. After careful consideration in retrospect, her parents and her school teacher said they considered her as being normally intelligent. Dr. Goldbloom, the consulting pediatrician, also considered her mentality and personality to be normal, although he made no elaborate study of this aspect of the case. A recent report from the mother, two years after an operation on the patient, states that the girl's memory is good and that she can read all the nursery books. The only abnormality of any sort that can be elicited is slight difficulty in the formation of sentences.

Convulsions began when she was 4 years old, when the right arm began to jerk one day while she was being dressed. This was accompanied with spasmodic forward movements of the pelvis. The attack was relieved by a hot bath. A second attack occurred three months later, and for the succeeding two years they occurred at intervals of three or four months. In her seventh year the interval between attacks had been reduced to three weeks, although the seizures were less severe. Nine months before her admission to the hospital a severe attack lasted for four hours.

In a typical attack the child awakened with a cry, and the right arm was raised above the head with clonic convulsive movements. The mouth was pulled to the right, followed by turning of the eyes and head to that side. When the convulsive movements ceased she was able to speak, even though the right arm remained paralyzed for a few minutes. There was never incontinence of urine during an attack. Occasionally she complained of headache on the left side associated with dizziness.

Physical Examination.—The patient was well developed, of normal size, intelligent and cooperative. The only abnormal findings were: oscillating nystagmus, rather marked on gaze to the left and upward; slight internal squint of the right eye; intention tremor of the right hand; slight deviation of the tongue to the right, and shortness (1 cm.) of the right leg.

Because the description of the attacks suggested a focus in the left motor cortex, encephalography was carried out, the spinal route being used (fig. 2*A*). The spinal fluid pressure was within normal limits (420 mm. of water) with the patient sitting. The encephalograms indicated an abnormal condition in the midline and led us at first to suspect a cyst of the cavum septi pellucidi.

Operation.—An osteoplastic craniotomy in the left parietal region was performed, and the left parietal lobe was retracted from the falx anteriorly. The anterior end of the corpus callosum came into view. It was penetrated with a ventricular needle, and cerebrospinal fluid was obtained from beneath it. With an open-ended needle tissue was removed from the corpus callosum. Microscopic study showed that this was white matter typical of the corpus callosum.

Comment.—When this patient was operated on the possibility of there being partial agenesis of the corpus callosum was not considered. The unusual ventriculogram was difficult to interpret, and at the time of exploration the most anterior aspect of the corpus callosum was the only region exposed without further explora-

tion. After patient S. van G. (case 2) had been studied, the ventriculograms in the two cases were recognized as identical in certain respects, and it became evident that the diagnosis in case 1 should have been partial absence of the corpus callosum, as will be pointed out in the discussion to follow. The salient features

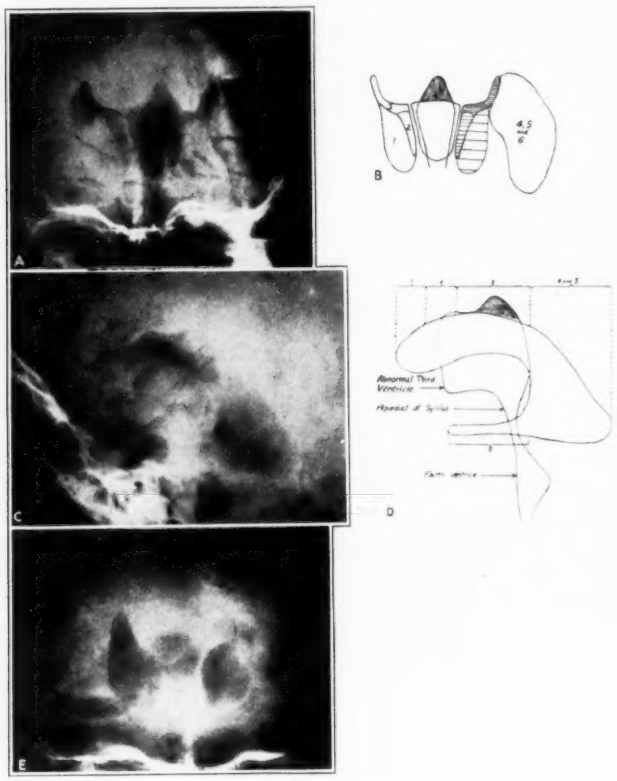

Fig. 2.—*A*, ventriculogram showing partial agenesis of the corpus callosum (case 1), anteroposterior view (brow up). The unusual features which characterize this ventriculogram are the wide separation of the anterior horns without a mesial filling defect of their outlines, the large body of air centrally placed and reaching much higher than a normal third ventricle and the bicornate appearance of the lateral ventricles. *B*, a diagrammatic representation of figure 2 *A*, labeled according to the ventricular subdivisions outlined in figure 4. The triangular shadow which is stippled in the diagram is posterior to the broader central shadow, as explained in the discussion. *C*, a ventriculogram in case 1, a right lateral view (left side up). The posterior horns are moderately enlarged. *D*, a diagrammatic representation of figure 2 *C*. The stippled portion of the third ventricle rises just posterior to the corpus callosum, which is absent from this point backward. *E*, a ventriculogram in case 1, an anteroposterior view (brow up) taken after a large portion of the oxygen had been absorbed so that only enough was left to fill the more anterior portions of the lateral and third ventricles. Only the broad portion of the central shadow now remains, indicating that the cavity producing this shadow is situated anterior to that which is stippled in figure 2 *B*.

of the ventriculogram were as follows: wide separation of the anterior horns, a large body of air centrally placed and reaching much higher than a normal third ventricle and a bicornuate appearance of the lateral ventricles (figs. 2*A* to *E*). Other features of the roentgenograms also will be discussed later.

CASE 2.—S. van G., a girl aged 18 months, was first seen in September 1933, chiefly because of epilepsy. Her birth had been normal, at full term, and there were no unusual feeding difficulties, though she never attempted to feed herself as she grew older. Food had to be placed in her mouth. There was nothing unusual in her manner, except that she seemed dreamy and would sometimes stare vacantly. She never attempted to crawl but sat up at the age of 6 months and walked at the age of 12 months. Dentition was normal. She had made no effort to speak and showed little interest in her surroundings and practically no interest in toys.

At 6 months of age the child first began to have petit mal attacks, consisting of turning the eyes and then the head to the right. The pupils became dilated and unresponsive to light. Sometimes the right arm would flex and the hand would clench, but in no attack was there a true convulsion or any muscular twitching. During the attack the face would become reddish purple, and the child usually vomited. The vomiting was occasionally projectile. The attacks usually lasted about a minute, and their frequency increased up to eight or nine in one day. Three months after the onset of the attacks the administration of phenobarbital was begun, ¼ grain (16 mg.) three times a day, which held the attacks in complete abeyance.

The patient had had none of the diseases of childhood. There had been no accidents, and the family history cast no light on the situation.

Examination.—The child was restless and continually in motion, whining most of the time, a drawling whine rather than the shrill cry of a normal child. She paid no attention to objects held before her. When placed on the floor she picked strings from the rug and placed them in her mouth. There seemed to be a preference for the use of the right hand. She walked with a somewhat waddling gait and with the body inclined forward. There was no suggestion of muscular spasticity, atrophy or weakness. When she attempted to grasp an object with either hand, the movement was slow and somewhat athetoid. The remainder of the examination revealed no abnormality, except that the palatal arch was high.

Two attempts to demonstrate the ventricles by the spinal route having failed, oxygen was injected directly into the ventricles. The ventriculogram revealed widely separated anterior horns and a broad central shadow which fused with the shadows of the lateral ventricles. The dense portion of the central shadow presented a definite corset-shaped outline (fig. 3).

The spinal fluid pressure was within normal limits.

Operation.—Because of the obvious abnormality shown in the ventriculograms, a small osteoplastic craniotomy was performed over the longitudinal fissure. When the right hemisphere was retracted from the falx, an extraordinary condition was encountered. Instead of a corpus callosum, only a translucent membrane bridged the bottom of the fissure. The membrane was obviously the pia-arachnoid and probably corresponded with the velum interpositum. When this membrane was incised, there came a gush of cerebrospinal fluid. The masses of the thalami and basal ganglia were more widely separated than usual. The corpus callosum and septum pellucidum seemed to be completely absent, but there was no other gross abnormaltiy to be seen, except the lateral displacement of the basal ganglia of each side and obvious enlargement of the ventricular system.

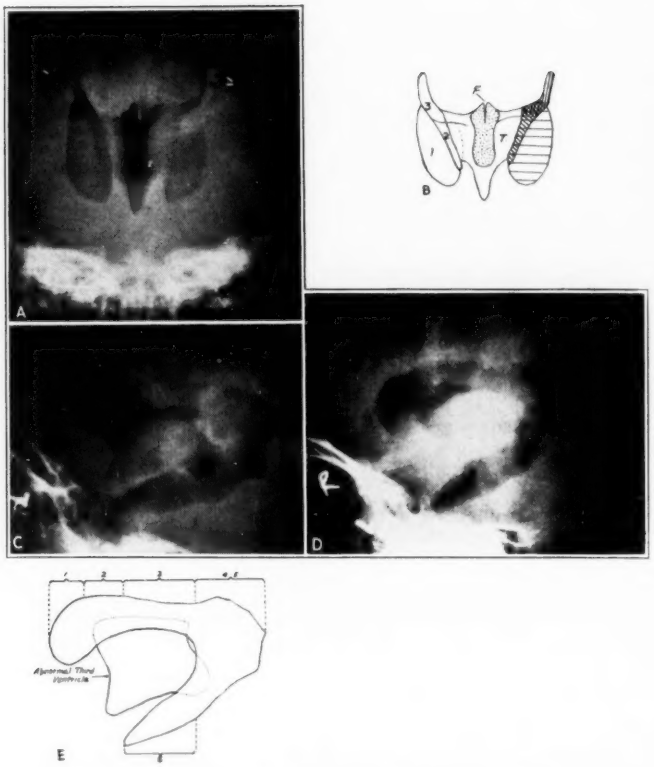

Fig. 3.—*A*, a ventriculogram showing complete agenesis of the corpus callosum (case 2), anteroposterior view (brow up). Note the wide separation of the anterior horns (portions 1), the narrowing of portions 2, the bicornuate outline of portions 3 and the moniliform shadow extending high in the midline. *B*, a diagrammatic representation of figure 3 *A*. *F* indicates impression of the falx. Portions 1, 2 and 3 of the lateral ventricles are shaded differently. *T* indicates broadening of the third ventricle anterior to the optic thalamus. *C*, a lateral ventriculogram in case 2 (left side up), showing an abnormally high extension of the third ventricle. Note the straight horizontal character of the superior margin of the third ventricle as compared with that in case 1 (figs. 2 *C* and *D*). *D*, lateral view (right side up), showing the anterior horn to better advantage than in figure 3 *C*. *E*, a diagrammatic representation of figures 3 *C* and *D* combined.

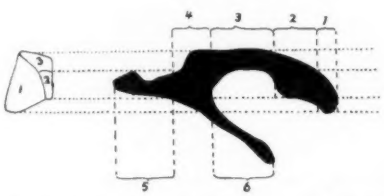

Fig. 4.—Diagram illustrating the method of ventriculographic analysis (from Torkildsen and Penfield [23]). Portions 1, 2 and 3 are seen in anteroposterior view at the left. 1 is the tip, which deviates laterally, 2 is mesial to the caudate nucleus and anterior to the thalamus and 3 is above the thalamus.

CASE 3.[22]—G. D., a man aged 21, was referred to one of us (W. P.) because of epileptic seizures in January 1935. Convulsive seizures had begun two years previously, being characterized by dizziness, sometimes associated with twitching of the right side of the face and right hand, but without loss of consciousness. On one occasion such an attack progressed to a generalized convulsion with loss of consciousness.

The patient was born at full term, forceps being used. He nursed normally and began to walk at 18 months. At the age of 2 years, after an illness of one month, it was observed that he limped with the right leg. The father, a physician, noted that the boy used the right arm less well than the left when he was 8 years old. The father and a brother being left handed, little importance was attached to this fact. The boy began to write with the left hand first but learned to write with either hand, preferring the left.

Fig. 5 (case 3).—Photograph of G. D.

The patient advanced normally in school. On entering the university, he failed in English and history but passed in chemistry, mathematics and physics. He was consequently taken from the university and placed in a business school.

Physical Examination.—The right arm and leg were smaller and shorter than the corresponding left extremities (fig. 5). The face showed no asymmetry, and the general examination otherwise gave normal results.

The visual fields, when carefully taken, showed no departure from normal; in fact, all the cranial nerves proved to be normal. The vestibular and cochlear reactions were found to be normal by Dr. W. J. McNally. The deep reflexes were normal and symmetrical, except that the right patellar reflex was a little more

22. This case and cases 4 and 5 have been added since the first two cases were described in June 1934.

active than the left. The abdominal reflexes were present on the left but less active than those on the right. The cremasteric reflexes and the plantar reflexes were normal. There was comparative weakness of the right arm and leg. No incoordination and no disturbance of sensation were found. A Wassermann test of the spinal fluid was negative.

In the general examination it was evident that the patient's responses were slower than normal but accurate. Dr. W. T. B. Mitchell made a careful psychologic examination of the patient; he summarized the results as follows:

"The psychometric examination indicates that the subject is of average intelligence for an adult. No particularly significant findings were revealed in the various tests. In the Binet-Simon examination, with the exception of practical planning, all tests were passed at the average level for an adult, and in addition the patient successfully passed the tests dealing with auditory memory and reversal

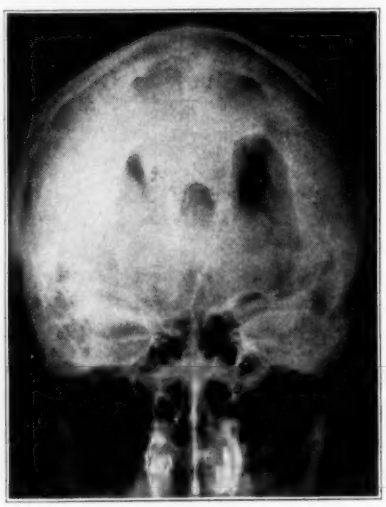

Fig. 6 (case 3).—Partial agenesis of the corpus callosum. Note the batwing outline formed by the height and the wide separation of portions 3 of the lateral ventricles. Some oxygen is present in the enlarged portion 4 of one side only.

of digits at the superior level for an adult. The score of the Monroe silent reading test indicated that both in reading and in comprehension of written material the patient's performance was at about the ninth grade level.

"A study of the general personality showed no frankly psychopathic findings. In a personal interview there was revealed a suggestive lack of self-confidence and drive and perhaps evidence of a lack in independent planning and decision. It is interesting to find some corroborative evidence of these lacks in the scores of the Bernreuter personality schedule."

Encephalograms were made after the spinal injection of 80 cc. of oxygen. This gave an appearance typical of absence of the corpus callosum, as in case 2. The left lateral ventricle was larger than the right, indicating atrophy of the left hemisphere, which must have been related to the patient's right hemiparesis. The third ventricle was wide with a rounded apex (fig. 6). The lateral ventricles were widely separated and greatly enlarged in their posterior extremities. The lateral

view of the third ventricle showed it to be excavated somewhat anteriorly, suggesting the possibility of a small rudimentary corpus callosum anteriorly.

Diagnosis.—Encephalography demonstrated congenital partial absence of the corpus callosum, enlargement of the lateral ventricles, most marked on the left, and comparative atrophy of the left hemisphere.

CASE 4.—H. D., a boy aged 2 years, was referred to one of us (W. P.) by Dr. Graham Ross in October 1935 because of retarded development. The delivery had been normal, at full term. The infant did not take feedings well. Up to the time of admission to the hospital the child had never been able to sit up, and he took little or no interest in his surroundings.

Examination.—The child's head was unusually high and broad from side to side, the occiput being flat and the frontal bosses prominent (fig. 7). Physical examination gave no unusual findings, except that the child showed no evidence of mental activity and could not sit up.

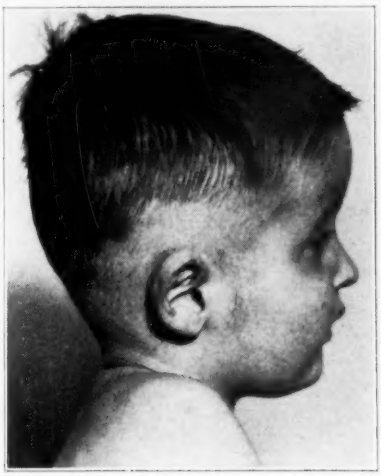

Fig. 7 (case 4).—Photograph of D. H.

Wassermann tests of the blood and spinal fluid were negative. The content of protein in the cerebrospinal fluid was 22 mg. per hundred cubic centimeters; the amounts of sugar and chlorides were normal. The cerebrospinal fluid pressure was normal.

After 130 cc. of oxygen had been injected into the spinal subarachnoid space, the roentgenograms gave the batwing appearance typical of absence of the corpus callosum (fig. 8). The impression of the falx could be plainly seen on the upper outline of the third ventricle. The third ventricle rose to a level several centimeters higher than normal. The extraordinary enlargement of the posterior horns of the lateral ventricles seen in the other cases was seen also in this case. The outline of the fourth ventricle was normal at its lower extent but became larger than normal as it passed upward to form the aqueduct of Sylvius.

Diagnosis.—The diagnosis was complete agenesis of the corpus callosum.

CASE 5.—S. S., a girl aged 5 years, was referred to one of us (W. P.) by Dr. J. M. J. MacPherson, of Campbellton, New Brunswick, Canada, on account

of petit mal epileptic seizures for the preceding sixteen months. At the time of the attacks the child would stand and gaze blankly or fall to the ground and then resume her previous activity without being aware of the interruption. Delivery had been normal. She began to talk at 11 months and to walk at 13 months. Two of the child's uncles had been committed to a hospital for patients with mental disease.

Examination.—There were no abnormal findings on general or neurologic examination. The Wassermann test was negative, and the cerebrospinal fluid was normal.

Encephalograms showed the ventricles to be large but symmetrical. The lateral ventricles otherwise presented a normal outline (fig. 9 *A*). The anterior aspect of the third ventricle was of normal width, but the posterior portion was much wider, and the posterior end curved upward like a tail. It thus passed posterior to and above the upper end of the aqueduct of Sylvius (fig. 9 *B* and *C*).

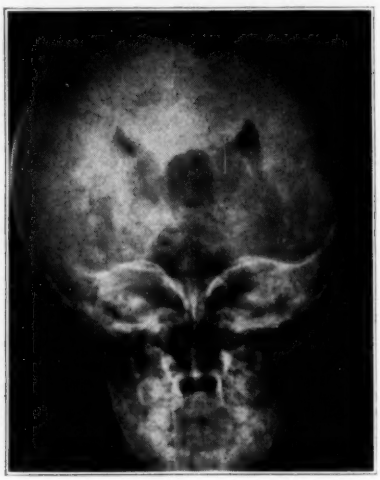

Fig. 8 (case 4).—Complete agenesis of the corpus callosum. The imprint of the falx is evident on the upper outline of the third ventricle.

Diagnosis.—The diagnosis was probable partial agenesis of the corpus callosum resulting in a defect of only the posterior portion of the corpus callosum or splenium.

VENTRICULOGRAPHIC FEATURES

Analysis of the ventriculograms is most easily made by reference to the ventricular subdivisions of Torkildsen and Penfield [23] shown in figure 4. Topographic references are made according to that outline.

In most of the reports of cases of agenesis of the corpus callosum in the literature, drawings and photographs have been included. In only one report, however, that of Bruce,[14] were the photographs adequate for a visualization of the ventricular contours. Sections of only the left half

23. Torkildsen, A., and Penfield, W.: Ventriculographic Interpretation, Arch. Neurol. & Psychiat. **30**:1011 (Nov.) 1933.

of the brain were pictured by Bruce, so that in figure 10 we have reproduced his photographs, together with a mirror image of each so as to aid in visualizing what the ventriculographic appearance of this specimen would have been.

The more anterior transection (fig. 1 *A*) cuts through portion 2 of the ventricles. Figures 1 *B* and *C* cut through portion 3, while figure 1 *D* shows the enlarged portion 4. The appearance in this case corresponded with that noted on opening the third ventricle at operation in case 2. "On separating the hemispheres," Bruce said in his autopsy description, "it was seen that this commissure (corpus callosum) was completely absent, as was also the psalterium of the fornix. Covering the third ventricle and the sides of the optic thalami was a thin mem-

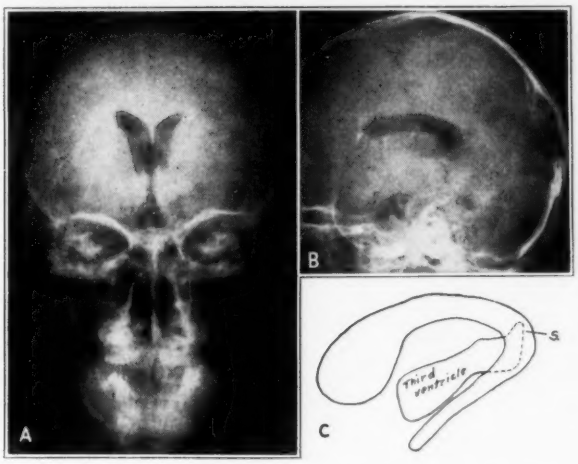

Fig. 9.—*A*, a ventriculogram showing partial agenesis (splenium only) of the corpus callosum (case 5). The film was taken with the brow up and shows the normal outline of the lateral ventricles and the increased depth of the posterior portion of the third ventricle. The anterior portion of the third ventricle could be seen to be normal in the films but is not deep enough to reproduce. *B*, a lateral film taken with the occiput up (case 5), showing oxygen in the posterior part of the third ventricle, which hooks upward and around the posterior end of the deficient corpus callosum. *C*, a diagram of the outline of the ventricles drawn from the whole series of roentgenograms in case 5. *S* indicates upward extension of the posterior aspect of the third ventricle, signifying absence of the splenium.

brane [24] (evidently the velum interpositum). This structure had extended into the lateral ventricles and was fringed by the choroid plexus in the usual way." He found the fornix just mesial to the lateral ventricle on each side (see fig. 10, *F*.). The anterior, middle and posterior

24. It was this membrane which was incised during the operation on our second patient.

commissures appeared normal, as well as the optic thalami, infundibulum and lamina terminalis. He described a zone of white matter (*S. P. T.*) containing nerve fibers which ran anteroposteriorly and which suggested an abortive effort at the formation of a callosal commissure. It is interesting that King and Keeler [9] found a similarly placed bundle of nerve fibers in some of the mice with total absence of the corpus callosum which they described.

In figure 10 *B* those structures which surround the third ventricle in its anterior portion are seen. This ventricle extends laterally into the callosal fissures and is limited by the fornices, which lie between it and

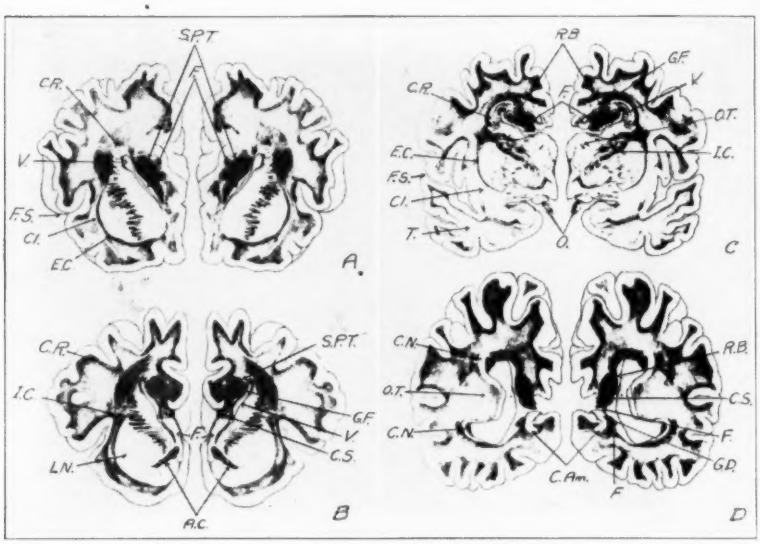

Fig. 10.—These four figures, modified after Bruce,[14] are frontal cross-sections of a brain with complete absence of the corpus callosum. The sections are arranged (*A* to *D*) from before backward. They are in reality negative reproductions, so that the white matter is represented in black. In *A*, *C.R.* indicates corona radiata; *F.S.*, fissure of Sylvius; *Cl.*, claustrum; *E.C.*, external capsule; *F*, fornix; *V.*, lateral ventricle, corresponding to portion 2 in figure 4; *S.P.T.*, zone of white fibers which run for the most part anteroposteriorly. In *B*, *I.C.* indicates internal capsule; *L.N.*, lenticular nucleus; *A.C.*, anterior commissure (said to be of normal size); *V.*, ventricle, corresponding to transition from portion 2 to 3; *G.F.*, gyrus fornicatus; *C.S.*, callosal sulcus; *F.*, fornix. In *C*, the transection was made posterior to that in figure 10 *B* through the optic thalamus. *T.* indicates temporal lobe; *O.T.*, optic thalamus; *O.*, optic tract; *R.B.*, posterior extension of the tract marked *S.P.T.* in figure 10 *A* and *B*. The bicornuate appearance of the ventricles is evident. *D* is a transection made posterior to that in figure 10 *C*. The ventricles were cut at the level of portion 4, showing the same posterior ventricular enlargement as in our cases. *G.D.* indicates fascia dentata; *C.Am.*, cornu ammonis; *R.B.*, posterior extension of the tract marked *S.P.T.* in figure 10 *A* and *B*; *C.N.*, tail of the caudate nucleus.

portion 2 of the lateral ventricle. The outline of the fornix may be seen in figure 2*A*. In figure 10*C* the more posterior portion of the third ventricle is seen. The moniliform outline seen in the ventriculogram in figure 3*A* is obviously produced by the inward bulging of the optic thalami. Further, the apparent communication between the lateral ventricles and the upper portion of the third ventricle in figure 10*C* corresponds closely with the horizontal shadows in figure 3*A*.

The leptomeningeal roof of the third ventricle, which has been removed, would have pressed upward against the free edge of the falx, as indicated by the filling defect at the apex of the third ventricle in figure 3*A*.

In all cases it is seen that the third ventricle extends abnormally high, but in case 1 the corpus callosum which is present anteriorly prevents as marked an upward extension as is seen in case 2. This is best seen in the anteroposterior view (fig. 2*A* and *B*). In all cases there is considerable widening of the third ventricle anteriorly, as though the absent fibers of the corpus callosum had allowed the basal ganglia to pull apart, while posteriorly the massa intermedia had held the walls more closely together.

As viewed anteroposteriorly, the anterior horns (portion 1) are normally shaped but wide apart, especially in case 2 (fig. 3*A*). Portion 2 is seen to be narrow on each side. Portions 3 are widely separated and rise high as they pass backward and outward, because of the absence of the roof of the corpus callosum. This gives the ventricular outline the peculiar bicornuate appearance seen anteroposteriorly. The tips of the horns are formed by portions 3 on either side. There is nothing unusual in the posterior and inferior horns of the ventricles, except that the posterior horns are very large (fig. 2*C*; compare also with Bruce's case, fig. 10*D*).

Differential Diagnosis.—A space-occupying mass situated between the lateral ventricles could cause a symmetrical separation of the anterior horns and bodies of the lateral ventricles. In this event, however, there would be a mesial filling defect in the midline which would outline the mass. A striking example of such a space-occupying mass is a cyst of the cavum septi pellucidi, or so-called fifth ventricle. Dandy [19] has recently reported two cases of this rare condition. The ventriculograms in these cases showed that the cyst had produced a mesial excavation as well as separation of the anterior horns. The midline cyst did not allow air to enter until its walls were ruptured.

A number of cases of enlargement of the cavum septi pellucidi have been reported. This congenital deformity may or may not be associated with hydrocephalus. It is usually associated with and often continuous

with an enlarged cavum vergae. Thompson [25] has reported a case in which there was exhibited ample communication between the large cavum and the third and lateral ventricles. He gave a comprehensive résumé of the literature, in which he included other cases of communicating cava. Were a ventriculogram to be made in such a case, one would expect to find the lateral ventricles symmetrically separated and a large body of air centrally placed and reaching higher than the third ventricle normally extends. We have had the opportunity of studying the specimen reported by Dr. Thompson in the museum of Professor Whitnall at McGill University. The unfortunate absence of the upper half of the brain precludes the possibility of accurately visualizing the contour of the superior aspect of the ventricles, but it is possible to conclude that the bicornuate appearance demonstrated in our cases could not have been produced by his specimen of enlarged communicating cavum.

Hence, except for the bicornuate appearance of the lateral ventricles, a communicating enlarged cavum septi pellucidi might present a ventriculographic appearance similar to those reported here. It is believed that the bicornuate appearance, in addition to the other characteristics, is the pathognomonic feature of agenesis of the corpus callosum.[26]

SUMMARY

The cases of five living patients presenting agenesis of the corpus callosum are reported, together with a description of the ventriculograms. Two presented complete and two partial absence of the commissure; one presented absence of only the splenium of the corpus callosum.

Analysis of the structures and the embryologic principles involved makes it possible to identify the lines of the ventriculographic shadows and to distinguish complete from incomplete agenesis.

The chief characteristics of the ventriculograms in the anteroposterior view are symmetrical separation of the anterior horns, with a moniliform shadow of gas between them which is continuous with the third ventricle below and rises higher than this ventricle should. Most striking of all is an almost right-angled shelving or bicornuate appearance of the bodies of the lateral ventricles. The latter, in our opinion, is pathognomonic of the condition.

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25. Thompson, I.: On Certain Abnormal Conditions of the Septum Pellucidum, Univ. California Publ., Anat. **1**:21, 1932.

26. In the light of this study the ventriculogram figured by Dandy in Dean Lewis' "Practice of Surgery" (Hagerstown, Md., W. F. Prior Company, Inc., 1930, vol. 12, p. 331) undoubtedly represents another case of agenesis of the corpus callosum.

REDUCTION OF POSTENCEPHALOGRAPHIC SYMPTOMS BY INHALATION OF 95 PER CENT OXYGEN

ROBERT S. SCHWAB, M.D.

JACOB FINE, M.D.
AND
WILLIAM JASON MIXTER, M.D.
BOSTON

The severity of the symptoms and the occasional serious effects following encephalography have interfered with the free use of this important diagnostic procedure. During the last three years there has been a general effort to make encephalography more certain, comfortable and safe. The use of the automatic continuous flow apparatus, originally worked out by Liberson in 1924 and made more efficient by von Storch in 1935, has reduced the number of immediate reactions and eliminated some of the failures associated with the old syringe method.[1]

In 1932 Davidoff and Dyke worked out a simple technic which consisted of using a minimum of air, carrying out the procedure in the x-ray room before the x-ray tube, taking x-ray pictures after 20 cc. of air had been injected and stopping the injection of air as soon as ventricular and subarachnoid filling was adequate.[2] They used a basal anesthesia obtained by means of amytal and morphine and one needle with a 5 cc. syringe. With their method the reactions were reduced in both duration and intensity.

By combining a modified continuous flow apparatus with the technic of Davidoff and Dyke we were able at the Massachusetts General Hospital to reduce appreciably the reactions in thirty consecutive cases.

The expenses for this investigation were supplied in part by the Permanent Charity Fund of the Harvard Medical School.

From the Neurological and Neurosurgical Services of the Massachusetts General Hospital and the Surgical Service of the Beth Israel Hospital.

Read at the meeting of the Boston Society of Psychiatry and Neurology, Nov. 21, 1936, and shown in exhibition form at the meeting of the American Neurological Association, Atlantic City, N. J., June 1936.

1. Liberson, F.: Apparatus for Simultaneous Displacement, Arch. Neurol. & Psychiat. **12**:300-304 (Sept.) 1924. von Storch, T. J. C.: Technique of Encephalography, Am. J. Roentgenol. **35**:78-92 (Jan.) 1936.

2. Davidoff, L. M., and Dyke, C. G.: An Improved Method of Encephalography, Bull. Neurol. Inst. New York **2**:75-94 (March) 1932.

With this technic, the patients still had headaches for two or three days, especially if they tried to get on their feet.

Schwab and von Storch have shown by cell counts on the spinal fluid at various intervals following encephalography that there is an intense pleocytosis, reaching a maximum in from twelve to eighteen hours (from 1,200 to 4,000 leukocytes per cubic millimeter) and then gradually subsiding with the slow absorption of air in the next forty-eight to seventy-two hours.[3] They found that the intensity of the cellular reaction was in direct relation to the amount of air used. N. L. Crone also observed this in his unreported work on the leukocytosis in the blood following encephalography.[4] Davidoff and Dyke found that the general reaction depended on the amount of air used.[2]

Removal of the air as soon as possible after satisfactory roentgenograms have been obtained, as is frequently done in ventriculography, with reduction in the reactions, would be the ideal approach to the problem of preventing postencephalographic symptoms. Direct aspiration is unfortunately not practically possible. Recent experimental and clinical studies by Fine, Frehling and Starr[5] have demonstrated that the inhalation of 95 per cent oxygen for a variable number of hours leads to a considerable acceleration in the speed of absorption of air from the body tissues or spaces, such as the subcutaneous fat, the fascial planes, the intestinal lumen and the peritoneal cavity. The purpose of this communication is to show the effect of breathing 95 per cent oxygen on the residual air following encephalography.

The principle in brief is as follows:

The alveolar gases contain approximately 79 per cent nitrogen, which exerts a partial pressure of 570 mm. of mercury. In the blood this pressure is slightly higher, while in the tissues it rises to approximately 630 mm. of mercury. The slightly higher tension of nitrogen in the tissues explains the slow diffusion of this gas into the blood and thence into the alveolar air under ordinary circumstances. By breathing 95 per cent oxygen the partial pressure of nitrogen in the alveolar air and therefore in the blood is reduced to nearly zero—thus increasing markedly the rate of diffusion of this gas from the tissues and thereby accelerating its absorption.

In encephalography, atmospheric air is placed in the subarachnoid and ventricular spaces. Here it is in contact with capillary and venous networks. The absorption of these gases by the blood depends on the

3. Schwab, R. S., and von Storch, T. J. C.: Cellular Reaction in the Spinal Fluid After Encephalography, New England J. Med., to be published.

4. Crone, N. L.: Personal communication to the authors.

5. Fine, Jacob; Frehling, S., and Starr, A.: Experimental Observations on Effect of 95 Per Cent Oxgen on Absorption of Air from Body Tissues, J. Thoracic Surg. **4**:635-642 (Aug.) 1935.

difference in the percentages of the gases in the subarachnoid space and in the blood. Usually after encephalography this difference is very slight—so slight in fact that the 80 to 120 cc. of injected air usually requires from forty-eight to seventy-two hours to be absorbed (figs. 1 and 2). If, however, 95 per cent oxygen is breathed, the nitrogen gas is mechanically washed from the lungs, and this causes the nitrogen dissolved in the blood to enter the lungs rapidly, so that in from twenty to thirty minutes the blood is nearly free from dissolved nitrogen. This nitrogen-free blood may then rapidly absorb the nitrogen gas in the cranial cavity. The oxygen fraction is, of course, rapidly picked up in any case because the venous and capillary blood can absorb from 30 to 40 cc. of oxygen per liter per minute.

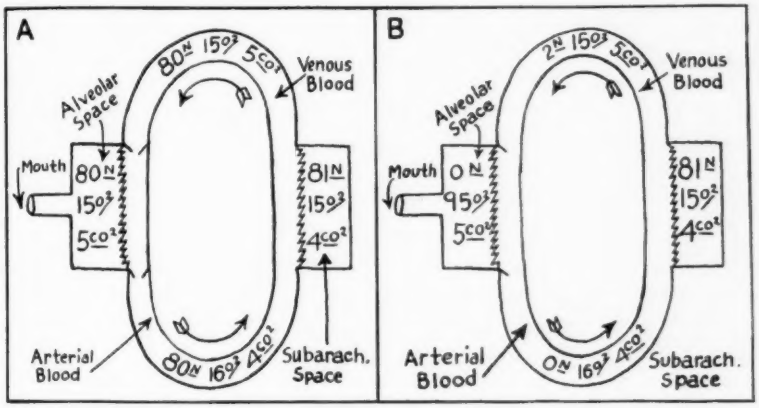

Fig. 1.—Diagrammatic scheme of the effect of 95 per cent oxygen on the absorption of air from the subarachnoid space; *A*, the removal of subarachnoid air when air is breathed; *B*, the removal of subarachnoid air when 95 per cent oxygen is breathed. *N* signifies nitrogen; O^2, oxygen gas; CO^2, carbon dioxide.

One would suppose at this point that since oxygen is so much more readily absorbed into the blood stream than nitrogen it could be used for the purpose of making encephalograms. If, however, pure oxygen is introduced into a body cavity such as the subarachnoid space, it acts exactly as it does in the alveolar space; e. g., it draws nitrogen gas out of the blood as it is itself absorbed. Hence, in a short while—from a half hour to an hour—pure oxygen in the subarachnoid space will be turned into a mixture of 13 per cent oxygen, 5 to 6 per cent carbon dioxide and 81 per cent nitrogen, and we are faced with the original situation that obtains when air is introduced. Owing to the fact that oxygen is more rapidly diffusible than nitrogen, there will be in this case a decrease in the gaseous volume of from 15 to 25 per cent. This fact alone, we

believe, would justify the use of pure oxygen instead of air—everything else being equal. For example, Penfield [6] has found this to be so in his clinic.

APPARATUS USED

In the original work with 95 per cent oxygen, after encephalography we used a specially built oxygen tent, using from 10 to 14 liters of oxygen per minute. We were able, with the small size of the tent and the large oxygen supply, to

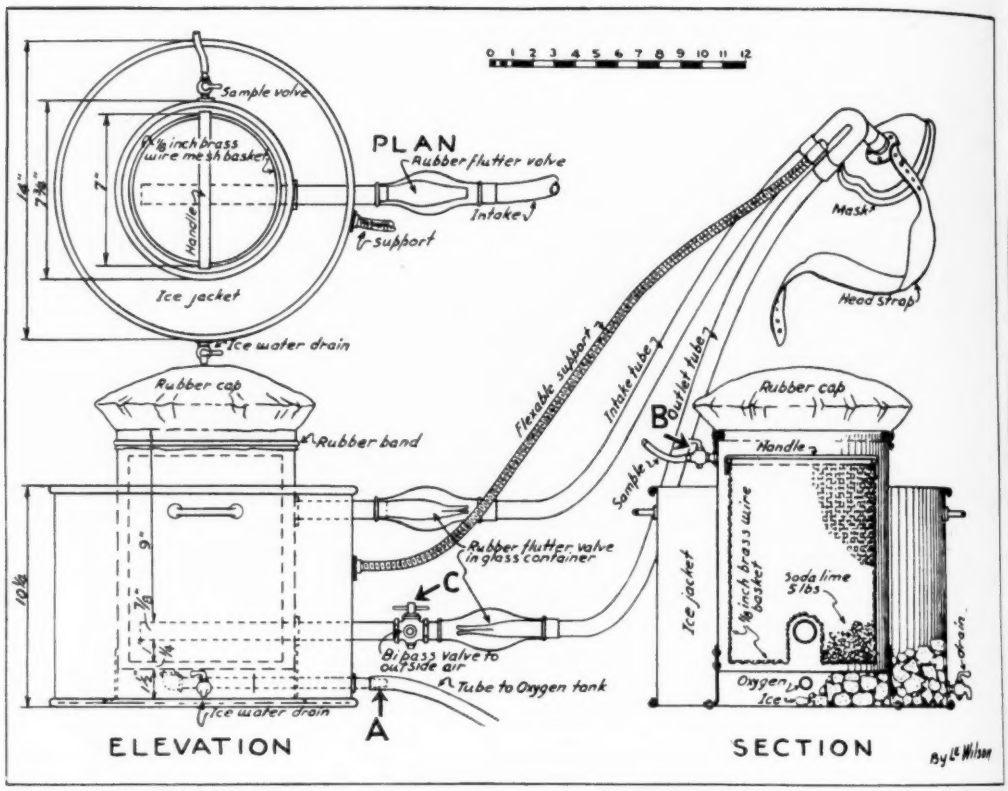

Fig. 2.—Diagram of the machine used for the administration of pure oxygen. Oxygen gas enters at *A*; samples for analysis are taken at *B*; the rest is like a basal metabolism test machine containing soda lime and rubber flutter valves. The by-pass at *C* allows the expired breath to escape into the atmosphere, carrying off the nitrogen gas.

reach 95 per cent oxygen in from twenty to thirty minutes. The cost of the gas and the complications of a tent with ice, motor, etc., made the procedure appear impracticable to some of us. Hence we developed a simple mask and gasometer (figs. 2 and 3).

6. Penfield, Wilder: Personal communication to the authors.

This apparatus[7] requires only five minutes to reach a saturation of 95 per cent oxygen; it has no motor and uses only 2 liters of oxygen gas per minute. Oxygen gas enters at the bottom; samples for analysis are taken through a small stopcock. The rest is like a basal metabolism test machine containing soda lime and rubber flutter valves. The by-pass to the left of the oxygen inlet is important, as it allows the expired breath to escape into the atmosphere, carrying off the nitrogen gas. This is turned on for the first twenty minutes and for three minutes every twenty to thirty minutes thereafter. During its use, the oxygen consumption must be raised to 6 or 7 liters a minute.

The apparatus is portable, easily cleaned and repaired, and its successful operation requires little skill. With a little supervised practice, a nurse can run it easily. One should watch it, but it does not require constant attention.

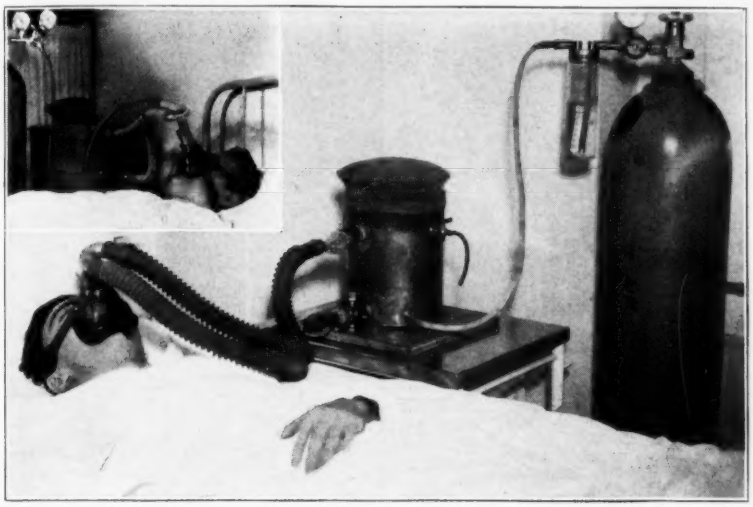

Fig. 3.—Photographs of the machine in use.

TECHNIC

The patient is given pentobarbital sodium, 1½ grains (0.19 Gm.), by mouth at intervals of one-half hour until he is fast asleep—a total of from 4½ to 7½ grains (from 0.39 to 0.58 Gm.); then ⅓ grain (0.02 Gm.) of a mixture of the hydrochlorides of the opium alkaloids or ⅙ grain (0.01 Gm.) of morphine sulfate and 1/150 grain (0.0004 Gm.) of scopolamine are given subcutaneously.[8] Food is, of course, withheld. The patient is brought on a litter to the x-ray room, where he is placed in a chair before the x-ray screen. Two lumbar puncture needles are introduced under procaine hydrochloride, and the continous flow apparatus is used. As soon as 50 cc. of air has been introduced a trial roentgenogram is taken. If filling is adequate, the apparatus is removed, and the usual eight x-ray pictures are

7. The apparatus is made by Warren E. Collins, Inc., 555 Huntington Ave., Boston.

8. The morphine or opium may be omitted if desired.

taken. If filling is not adequate more air is introduced. The required amount varies from 60 cc. to 240 cc. After the roentgenograms are taken the patient returns to his room and is placed immediately in the oxygen machine. At this point, 1 cc. of solution of posterior pituitary is given intramuscularly to increase the formation of spinal fluid to replace the disappearing air.

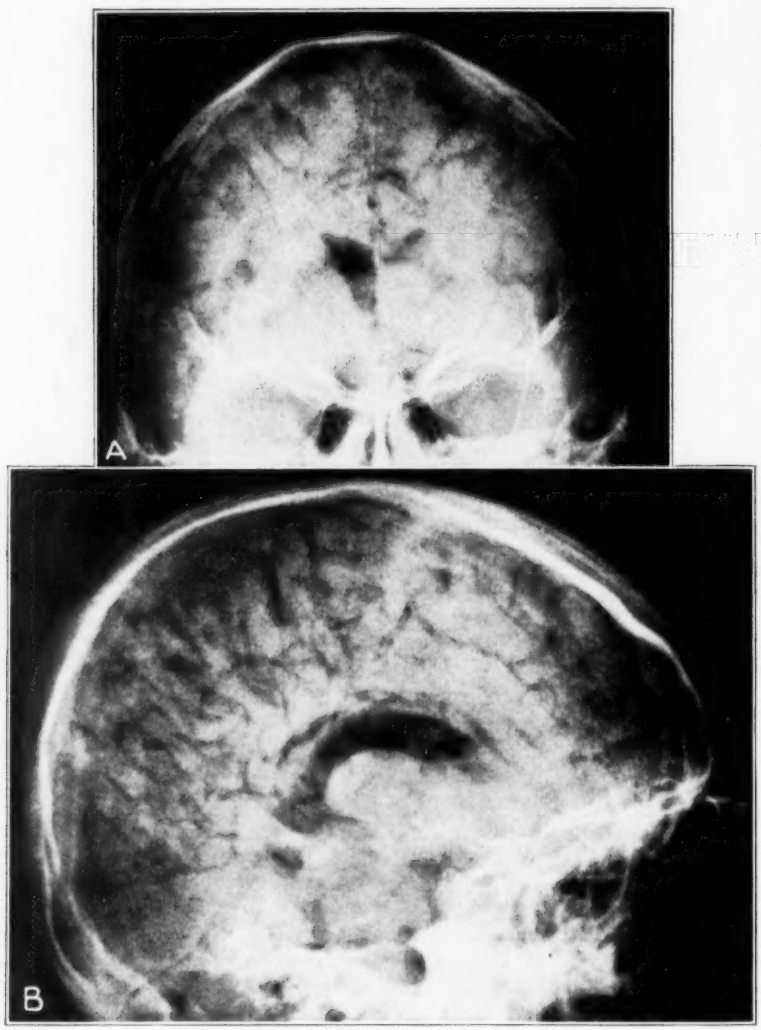

Fig. 4.—*A*, anteroposterior encephalogram before inhalation of oxygen was used; *B*, lateral encephalogram before inhalation of oxygen was used.

The patient remains in the machine for three hours. During this time there is usually observed a slowing of the pulse to 60 as the percentage of oxygen reaches 95. This bradycardia ordinarily persists only for from one-half to one hour

and then disappears. When the patient is taken from the machine he is usually conscious and surprisingly comfortable, and rarely requires further medication.

In fourteen cases we took a lateral and an anteroposterior roentgenogram of the skull after the three hour period in the machine; in all fourteen cases there

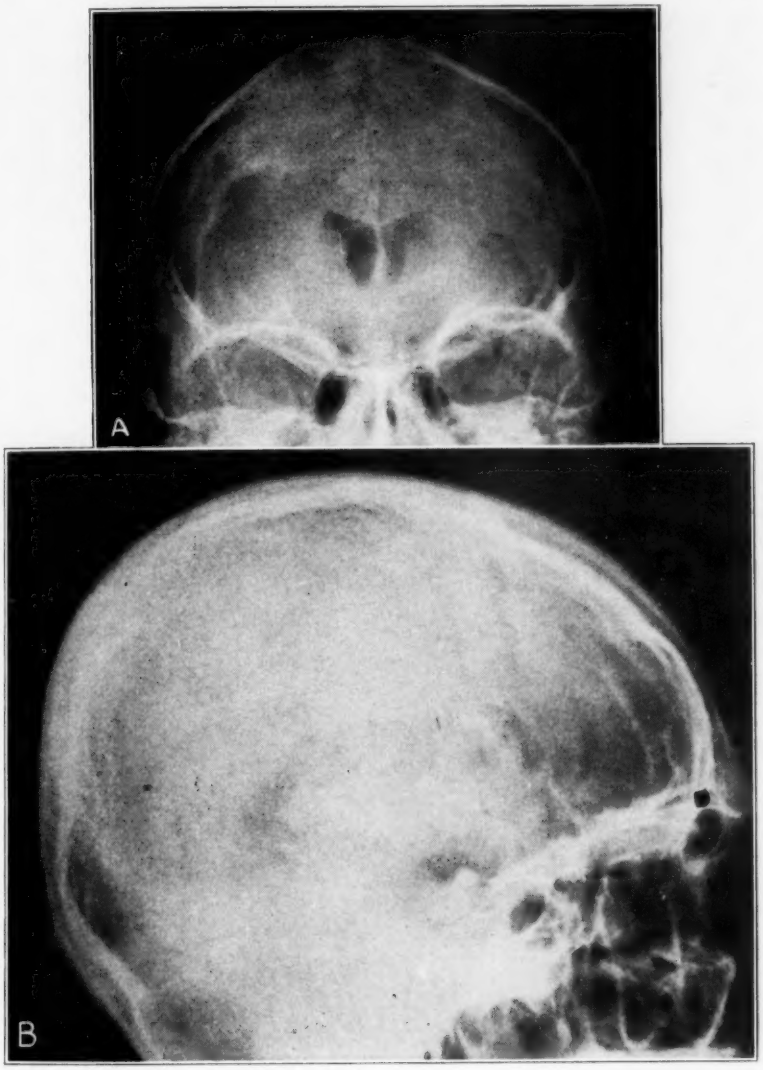

Fig. 5.—*A*, anteroposterior encephalogram in same case as the encephalogram shown in figure 4*A* after inhalation of pure oxygen (95 per cent oxygen) for three hours; *B*, lateral encephalogram in same case as the encephalogram shown in figure 4*B* after inhalation of pure oxygen (95 per cent oxygen) for three hours.

was nearly complete removal of the subarachnoid air. In six cases, no pictures were taken. In four, oxygen gas was injected instead of air, and the patient was not placed in the machine. In six control cases roentgenograms were taken at

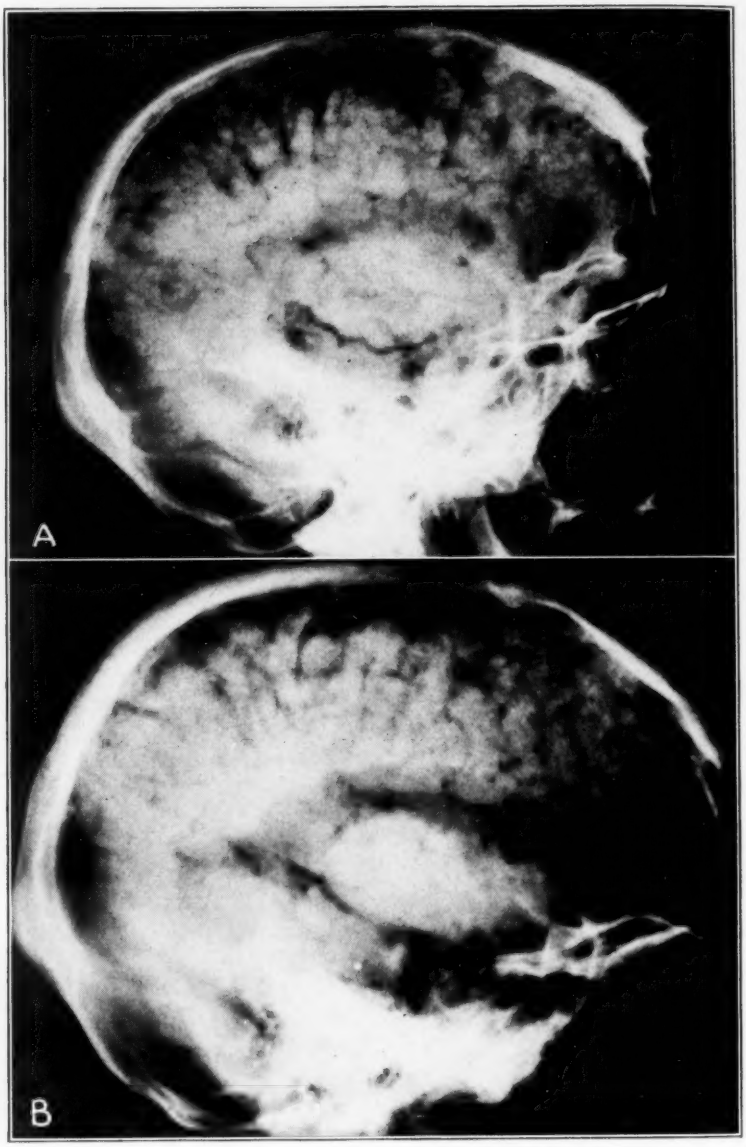

Fig. 6.—*A*, lateral encephalogram in control case; *B*, lateral encephalogram in control case three hours later (no oxygen inhaled). See figure 7.

three hours, and the patient was *not* placed in the machine. In ten cases oxygen gas was injected, and the oxygen machine was used as well. This group of patients had a slightly better recovery than those with whom air and the oxygen machine were used. The three hour pictures for the six of this group whose pictures were taken were not different from those in cases in which air was used. A summary of the forty cases is given in the accompanying table.

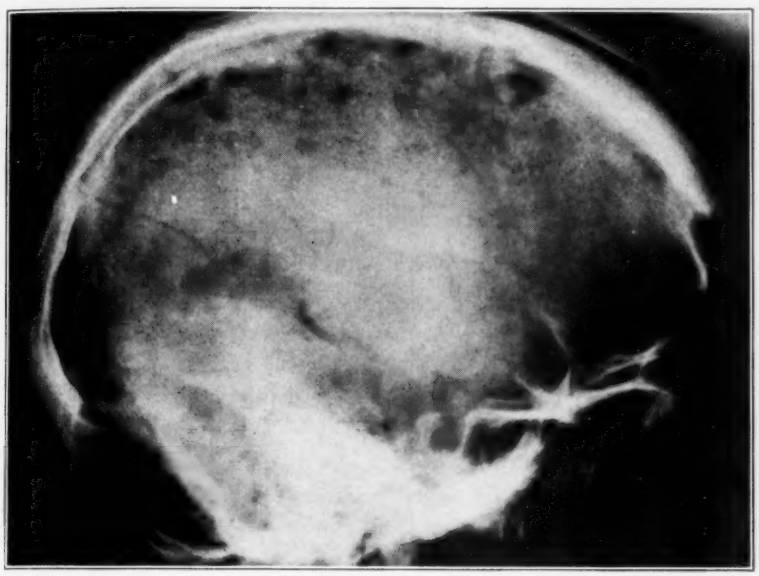

Fig. 7.—Lateral encephalogram in control case forty-eight hours later, showing some air still present.

Summary of Encephalographic Data

Procedure	Cases	Average Number Cc. of Gas Injected,	Encephalograms at 3 Hours	Subarachnoid Gas Present at 3 Hours	Average Number Days to Comfort	Average Number Days to Disappearance of All Symptoms
Air injected and machine used	20	101	14	All gone in 12; nearly gone in 2	1	2½
Air injected and machine not used	6	105	6	Most of gas present	2½	5½
Oxygen injected and machine used	10	135	4	None	1	2
Oxygen injected and machine used	7*	150	2	None	1	2-3
Oxygen injected and machine not used	4	140	4	Slight reduction visible in gas	2	3½
Total number for which machine was used					37	
Total number of controls					10	
Total					47	

* This series is from the Boston Psychopathic Hospital, by permission of Dr. C. MacFie Campbell. The other cases are from the Neurological and Neurosurgical Service of the Massachusetts General Hospital.

COMMENT

A study of the table shows that the inhalation of oxygen was followed by a prompt removal of most of the subarachnoid air during the three hours the patient was in the machine. All of our fourteen three hour pictures showed satisfactory reductions in the air. The air does not return, as shown by the pictures taken fifteen hours later. In only one case was all the air removed from the ventricles; it was greatly reduced in the others. The disappearance of the subarachnoid air was complete in twelve of the fourteen cases and nearly so in two.

The procedure resulted in no pulmonary complications. The bradycardia during the first hour was observed in most cases. There were no significant changes in the blood pressure, respiration or color of any patient in the machine. In nearly all cases the medication was sufficient to keep the patient quiet during the three hours in the machine.

We believe that the reactions were reduced in most cases. We believe that in eight of the cases reactions were minimal and were unusually short for encephalography.

If very small amounts of air or oxygen are used—from 30 to 50 cc.—in the encephalogram, as recommended by Davidoff and Dyke,[2] the benefits of this technic are of doubtful value.

Lumbar punctures made after the use of the oxygen machine showed a less cellular reaction than when it was not used.

We find that the large size oxygen tank can be used for twenty patients, the procedure using about 100 pounds (45.4 Kg.) of gas.

It is well to have a good gas analyzer on hand for testing the machine gas, because if 95 per cent is not reached the absorption of air will be slowed up. Even a small leak in the machine or in the tubes will reduce the concentration to 80 per cent. This is, however, not essential and, with reasonable care, can be omitted.

We find that the use of solution of posterior pituitary hastens the return of cerebrospinal fluid and reduces the headache. We failed to use it in four cases, and the pictures showed the same reduction of the air, but the clinical improvement was less noticeable.

A second model of the machine was made for use in the Boston Psychopathic Hospital. This had as an improvement an outside metal jacket in which ice or cold water could be placed to cool the gas used. Equally good results were obtained in the seven cases in which it was used. The cooling of the gas had no demonstrable effect, and it is not certain whether this added complication is really necessary.

This machine can be easily adapted so that it can be used for the administration of oxygen to patients with pulmonary or cardiac disease or for the brief use of 5 per cent carbon dioxide and oxygen.

SUMMARY

The inhalation of approximately pure oxygen gas (95 per cent oxygen) leads to the removal of all of the subarachnoid air following encephalography and most of the ventricular air in three hours.

When this procedure is followed, the headache and other reactions are reduced, as shown by the results in thirty-seven cases.

By injecting oxygen gas for the encephalogram and requiring the patient to inhale the pure gas for three hours afterward a still better result is obtained.

A simple apparatus for the administration of pure oxygen is described.

No complications of a pulmonary or cardiac nature follow the use of this procedure.

DISCUSSION

DR. TRACY PUTNAM, Boston: This is an ingenious method of removing air from the subarachnoid space. Anything that will do this is well worth while. All that I have learned from encephalography has been from Dr. von Storch. In regard to pressure relationships: Dr. von Storch showed that, contrary to one's expectations, air decreases pressure, and this may be responsible for some of the symptoms—if the air is extracted what happens to the pressure of the spinal fluid? The use of carbon dioxide or oxygen is perhaps of questionable value because so much is likely to escape before pictures are taken. Certainly it is unwise to move the patient from the operating room to the roentgenographic room. In regard to the extraction of gas, and this is an effective measure: Does it decrease the intracranial pressure? Is it possible that decrease in pressure rather than cellular reaction in the subarachnoid space causes the discomfort? Could this be alleviated by the use of a hypotonic saline solution, as well as solution of posterior pituitary?

DR. SAMUEL EPSTEIN, Boston: I think that Dr. Schwab's method is an important one. My associates and I have tried it at the Boston Psychopathic Hospital, with Dr. Schwab's help, and we also found that air was absorbed more quickly. In the course of our recent encephalographic work, we encountered something unusual. In the particular case to which I refer, important data were obtained from two to four days after encephalography. The roentgenograms which were taken immediately after the injection did not show much pathologic change, but without any inhalation of oxygen, such as Dr. Schwab describes, we took more roentgenograms of the patient's head two and four days afterward. We were surprised to find a great deal of pathologic change in the later pictures—we might have missed these observations. The case is unusual and is, I suppose, an exception to the rule. In most of the cases no air is shown in from four to five days after encephalography.

DR. WILLIAM HOLT, Boston: The only additional comment I wish to make is: In the anteroposterior view, three hours after encephalography, there was a striking reduction in the amount of air seen in the ventricles but no change in subarachnoid filling. For the succeeding three hours my colleagues and I used Dr. Schwab's apparatus, and there were a slight further absorption of air from the ventricles and apparently complete absorption of subarachnoid air. The apparatus used by Dr. Schwab does remove air from the subarachnoid space, but there is no striking change in the ventricular filling.

Dr. James C. White, Boston: Dr. Penfield uses pure oxygen in taking all his ventriculograms and encephalograms. The reactions in his patients were much less upsetting. I was on the point of trying the method here when Dr. Schwab began his work. When the patient breathes pure oxygen afterward there should be less reaction than when oxygen alone is used. The results I have seen in Dr. Schwab's cases are superior to those obtained in Montreal. Oxygen is converted to air in the subarachnoid spaces, and rebreathing should therefore be used afterward.

Dr. James B. Ayer, Boston: I wish merely to emphasize the relative comfort of this procedure over that of the methods used in the past and the quick comeback of the patient. The old method of introducing from 40 to 50 cc. of air caused the patient to vomit and sweat excessively afterward. All one got usually was poor roentgenograms, and the patient was prostrated. Now the procedure is carried out with a great deal of comfort and without the patient's knowledge. He is in excellent condition the same day. All this is the result of the continuous flow method and the procedure of getting rid of the air. In regard to Dr. Epstein's results: My associates and I took roentgenograms one, two or three days afterward, and it was unusual to find air visible on the third day. I consider that it is exceptional. How much pathologic change is there in fact? I doubt whether in more than one of two hundred cases one would observe anything in three or four days if there was proper filling at the start. We do not always obtain this, but lately it is much more frequent.

Dr. Jason Mixter, Boston: I wish to give every credit to Dr. Fine and Dr. Schwab in this investigation. I have followed the work with great interest but can claim no part of it for myself.

Dr. Robert Schwab, Boston: In answer to Dr. Putnam's question: We have tried to keep the pressure constant during the injection. When air is used the pressure falls slowly. In injecting oxygen we found we had to use from 50 to 60 cc. more gas than when air was employed, in order to maintain a constant intracranial pressure. We performed lumbar puncture on five patients after the oxygen machine had been used. The punctures were made approximately five hours after the air was first introduced. In two patients we found normal and in three subnormal pressures. Solution of posterior pituitary had been used in all these cases. The cellular reaction was between 350 and 500 cells per cubic millimeter—somewhat less than that which von Storch and I observed at a comparable time when the air was left in. In answer to Dr. Epstein's question: I asked Dr. Cornelius Dyke, of New York, and Dr. Aubrey Hampton, of Boston, about the value of leaving the air in the ventricles for later pictures. They expressed the belief that subsequent films show air in various uncertain places and that these residual bubbles may lead one seriously astray. With reference to Dr. White's remarks about the work of Dr. Penfield: Dr. Penfield wrote me a few weeks ago that he was using oxygen in cases of tumor and air for therapeutic encephalography. The removal of the gas by the machine is certainly not the last word, but we believe that it is an important step in making this important procedure more comfortable for the patient.

ANOMALOUS COMMISSURE OF THE THIRD VENTRICLE (ABERRANT DORSAL SUPRA-OPTIC DECUSSATION)

A REPORT OF EIGHT CASES

A. R. VONDERAHE, M.D.
CINCINNATI

An examination was made of the third ventricle in 371 human brains removed at autopsy at the Cincinnati General Hospital. In 8 instances an anomalous commissure connecting the lateral walls of the third ventricle was observed, making an incidence of approximately 2.15 per cent.

Grossly, these brains, fixed in a solution of formaldehyde, present a yellow thread about 1 mm. in diameter traversing the third ventricle and joining its walls. In sections from the frontal lobe the structure is found in the plane which passes between the anterior commissure and the posterior portion of the optic chiasm. In a ventrodorsal aspect of the third ventricle in this plane it lies at slightly varying distances from a middle level. In one instance the commissure was composed of two fine filaments (fig. 1).

For microscopic study, 6 of the specimens were sectioned serially in the frontal plane. Of these, 3 were prepared according to Morgan's iron-alum hematoxylin method, 2 according to the Weigert-Pal method and 1 according to the Bielschowsky method. Two of the specimens were sectioned serially in the horizontal plane and stained according to Morgan's method.

Microscopically, the structure is composed of finely medullated and nonmedullated fibers covered on the surface by a layer of ependyma. Occasional small blood vessels appear between the fibers. The fibers, in Weigert preparations especially, can be traced to that component of the dorsal supra-optic decussation (Ganser's commissure) which lies between the fornix and the lateral wall of the ventricle (fig. 3). As the fibers approach the commissure, they swing medially, enter it and are subsequently lost in the paraventricular nucleus of the opposite side. Greving [1] illustrated the components of the normal dorsal supra-optic

From the Department of Anatomy (Neurology), University of Cincinnati, College of Medicine.

1. Greving, R.: Die zentralen Anteile des vegetativen Nervensystems, in von Möllendorff, W.: Handbuch der mikroskopischen Anatomie des Menschen, Berlin, Julius Springer, 1928, vol. 4, p. 1026.

decussation (fig. 4). The anomalous commissure presented in this figure appears to be composed of fibers from the medial bundle of the dorsal supra-optic decussation which, instead of descending and crossing in the region of the chiasm in the usual manner, go directly across the ventricle to the opposite side.

The contiguous cells of the paraventricular nucleus are oriented in the direction of the commissural fibers, and the structure does not extend

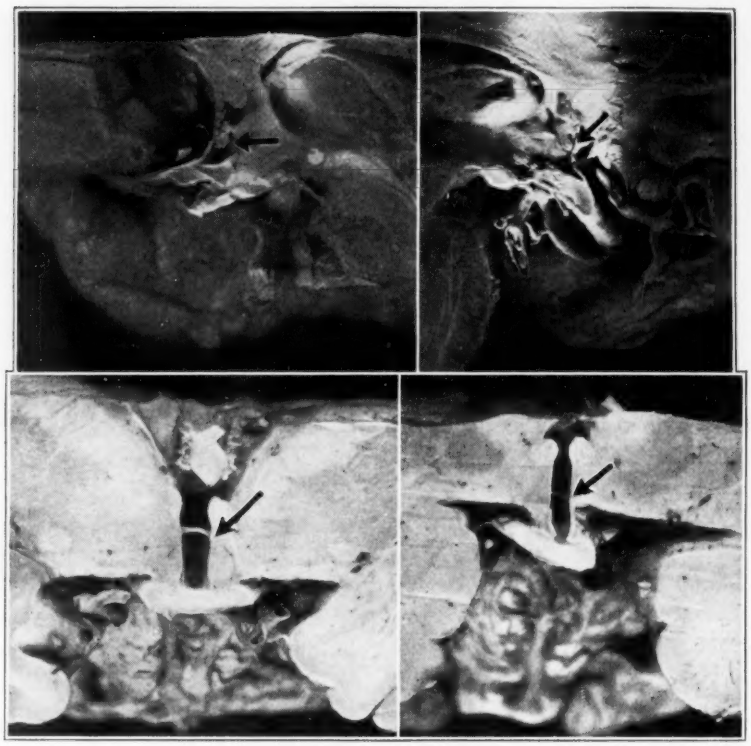

Fig. 1.—The arrow indicates the position of the commissure in sagittal or frontal sections of four brains.

in any instance beyond the oral or caudal plane of the paraventricular nucleus. The commissure contains from occasional to numerous cells of the paraventricular nucleus. In 1 instance (fig. 2 *A* and *B*) the cells of the paraventricular nucleus were so numerous that the commissure amounted to a fusion of these nuclei across the midline. For these reasons it was regarded as intimately associated with the paraventricular nucleus.

Of the 8 cases, 4 occurred in white persons and 4 in Negroes, 4 in males and 4 in females. It is interesting to note, however, that in 5 of

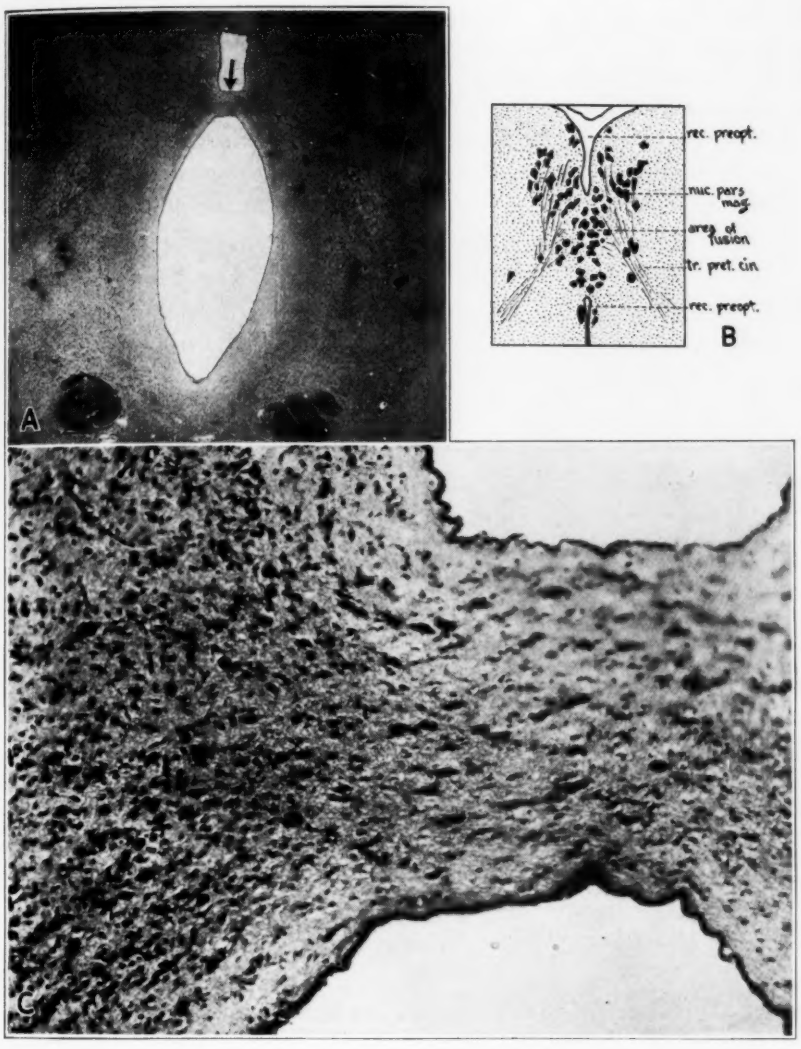

Fig. 2.—*A*, the arrow indicates the commissure in horizontal section. The cells of the paraventricular nucleus are faintly visible in the commissure and in a winglike distribution on either side (Morgan's stain). *B*, fusion of the paraventricular nuclei (nucleus preopticus pars magnocellularis, *nuc. pars. mag.*) is a constant finding in the angler fish, Lophius piscatorius (from Charlton). *C*, a higher power magnification of the same specimen illustrated in *A*, showing the distribution of the cells of the paraventricular nucleus throughout the commissure.

the instances the anomaly was associated with neoplastic growth elsewhere in the body; 3 of the neoplasms were malignant and 2 benign. Of the latter, both were related indirectly to the cause of death. In 1 instance death followed an operation for uterine myomas, and in the other instance an adenoma of the prostate gland was associated with extreme hypertrophy and diverticulosis of the bladder.

An inquiry was made into the sources of possible earlier descriptions of this anomaly, but no reference could be found. Comparative anatomic

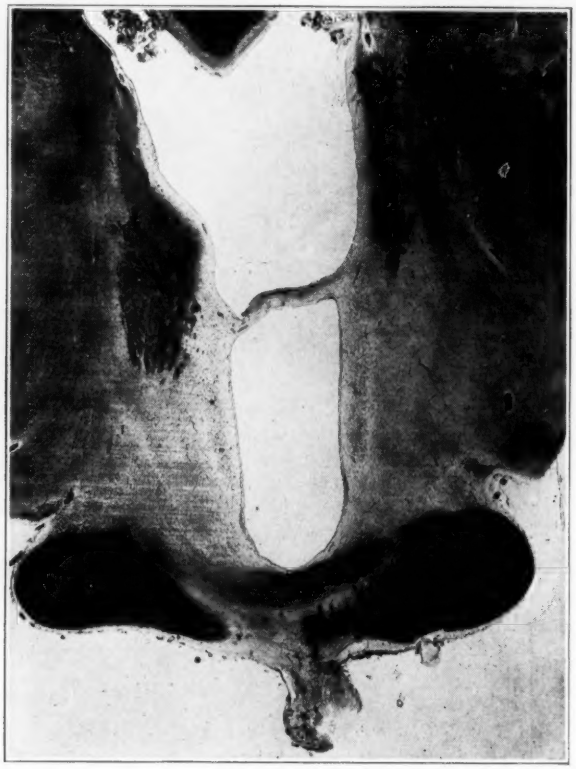

Fig. 3.—The fibrous character of the commissure is shown. The dorsal and ventral supra-optic decussations are shown. Weigert-Pal stain. Compare with figure 4.

studies, however, suggest some analogies. Most interesting in this connection is the observation of Charlton,[2] in a study of the paraventricular nucleus (nucleus preopticus, pars magnocellularis) in 140 fish

2. Charlton, H. H.: Comparative Studies on the Nucleus Preopticus Pars Magnocellularis and the Nucleus Lateralis Tuberis in Fishes, J. Comp. Neurol. **54**:237 (Feb.) 1932.

brains of various species. In the deep sea angler fish, Lophius piscatorius, a fusion of the paraventricular nuclei occurs across the third ventricle (fig. 2 *B*). The finding is apparently constant for this species. In the lamprey eel, Myxine glutinosa, Jansen [3] described as a constant finding the fusion of the hypothalamic nuclear groups, including the paraventricular nucleus (nucleus preopticus, pars magna cellularis), across the third ventricle, almost obliterating the cavity. This fusion, however, Conel [4] noted, occurs fairly late in the course of embryonic development; in earlier phases of embryonic life the hypothalamic por-

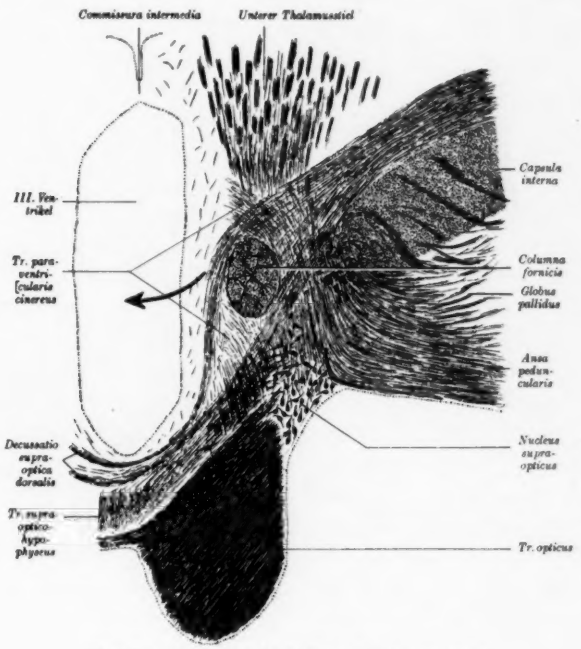

Abb. 111. Horizontalschnitt durch die Zwischenhirnbasis. Silberfärbung nach SCHULTZE. (Über Abb. 103 gelegen.) Zeichnung.

Fig. 4 (Greving).—The components of the dorsal supra-optic decussation. Those fibers of the dorsal supra-optic decussation which pass between the column of the fornix and the lateral wall of the third ventricle are regarded as probably contributing their fibers to the anomalous commissure. The course of these aberrant fibers is indicated by an arrow added to the original drawing.

tion of the ventricle is present. It may be recalled in this connection that the neural tube, of which the third ventricle is merely a modification, is one of the earliest of all developments and that any communication across it must of necessity be a fairly late manifestation.

3. Jansen, Jan: The Brain of Myxine Glutinosa, J. Comp. Neurol. **49**:359 (April) 1930.

4. Conel, J. L.: The Development of the Brain of Bdellostoma Stouti: External Growth Changes, J. Comp. Neurol. **47**:343 (April) 1929.

SUMMARY

Eight instances of an anomalous commissure of the third ventricle are described. The commissure is intimately related to the paraventricular nucleus. The cells of the paraventricular nucleus are found in it in greater or less number. The fibers which pass through it appear to be associated with the dorsal supra-optic decussation (Ganser's commissure). A study of the anomaly suggests that some of the fibers of the dorsal supra-optic decussation enter the paraventricular nucleus of the opposite side, thus pointing to a probable termination of these fibers in normal brains. The patients are evenly divided with respect to race and sex, but in five cases the anomaly was associated with neoplastic growths elsewhere in the body—malignant tumor in three and benign tumor in two.

AUTONOMIC INNERVATION OF THE EYELIDS AND THE MARCUS GUNN PHENOMENON

AN EXPERIMENTAL STUDY

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ROBERT A. GROFF, M.D.

AND

FRANCIS C. GRANT, M.D.

PHILADELPHIA

The present experimental investigations were suggested by an interesting clinical observation. One of us (F. C. G.)[1] recently reported a case in which chewing movements were accompanied by an involuntary elevation of the upper eyelid and the condition was completely relieved by section of the motor root of the fifth nerve. This reaction, known as the Marcus Gunn phenomenon, is characterized by ptosis, usually congenital, of the affected eye and by slow elevation of the upper eyelid synchronous with chewing movements.

Two principal theories have been advanced as an explanation for the mechanism of the phenomenon. One theory suggests a cortical pattern, in analogy with the Bell phenomenon; the other implies a connection between the medullary nuclei of the third and those of the fifth cranial nerve. Neither of these theories was satisfactory to us, since it was demonstrated in the case reported that the associated movements described were completely abolished by section of the motor root of the trigeminal nerve. Obviously, neither the cortical reflex arc nor a possible internuclear connection could have been affected by extramedullary section of the fifth nerve. Furthermore, in this patient associated movements of the upper eyelid could be produced by forcible, passive movements of the jaw after, as well as before, operation. This last observation suggested a proprioceptive reflex arc, the sensory pathway of which presumably runs in the sensory portion of the third division of the trigeminal nerve. However, the motor part of the arc is unknown.

This work was aided by a grant from the Rockefeller Foundation.

Read at the Sixty-Second Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 3, 1936.

From the Neurosurgical Clinic, the Hospital of the University of Pennsylvania, and the Harrison Department of Surgical Research, the University of Pennsylvania School of Medicine.

1. Grant, F. C.: The Marcus Gunn Phenomenon: Report of a Case with Suggestions as to Its Relief, Arch. Neurol. & Psychiat. **35**:487-500 (March) 1936.

The information gained from the literature and from the aforementioned case points to the autonomic system as a factor in the phenomenon. In all cases reported weakness of the homolateral third nerve was present. Contraction of the levator palpebrae muscle was definitely slow. Instillation of homatropine hydrobromide suspended the associated movement, while injection of procaine hydrochloride increased the ptosis. Both procaine hydrochloride and atropine are antagonists to acetylcholine in their action on the autonomic nervous system. These features are part of the so-called pseudomotor phenomena of Vulpian, Heidenhain and Sherrington.

Philipeaux and Vulpian [2] in 1863 showed that five days after section of the hypoglossal nerve mechanical and electrical stimulation of the lingual or of the chorda tympani nerve induced slow contraction of the tongue. Heidenhain [3] in 1883 corroborated this observation and was able to produce the reaction also by injection of nicotine. He applied to it the term "pseudomotor reaction." His co-worker Rogowicz [4] demonstrated that a similar reaction can be obtained in the lips by stimulation of the ansa Vieussenii (ansa subclavia) after previous section of the facial nerve. This curious type of movement was accurately described for the first time in Heidenhain's paper. The movements are characterized by a relatively slow contraction and relaxation, with a long latent period, and they continue for a time after the stimulus has been stopped. Sherrington [5] in 1894 proved conclusively that an excellent preparation is obtained by cutting the anterior and posterior roots of the lumbosacral region of the cord and subsequently stimulating the peripheral stump of the divided sciatic nerve. The reaction produced is a slow dorsal flexion of the foot, which continues for five seconds after cessation of the stimulus.

Frank, Nothmann and Hirsch-Kauffmann [6] attacked the problem from a different standpoint. They showed that the pseudomotor phenomenon can be produced by comparatively small doses of acetylcholine and that it is inhibited by epinephrine, procaine hydrochloride

2. Philipeaux, J. M., and Vulpian, A.: Note sur une modification physiologique qui se produit dans le nerf lingual par suite de l'abolition temporaire de la motricité dans le nerf hypoglosse de la même côté, Compt. rend. Acad. d. sc. **56:** 1009-1011, 1863.

3. Heidenhain, R.: Ueber pseudomotorische Nervenwirkungen, Arch. f. Physiol., supp., 1883, pp. 133-177.

4. Rogowicz, N.: Ueber pseudomotorische Einwirkung der Ansa Vieussenii auf die Gesichtmuskeln, Arch. f. d. ges. Physiol. **36:**1-11, 1885.

5. Sherrington, C. S.: On the Anatomic Constitution of Nerves of the Skeletal Muscles, with Remarks on Recurrent Fibres in the Ventral Spinal Nerve-Roots, J. Physiol. **17:**211-258, 1894.

6. Frank, E.; Nothmann, M., and Hirsch-Kaufmann, H.: Ueber die "tonische" Kontraktion des quergestreiften Säugetiermuskels nach Ausschaltung des motorischen Nerven, Arch. f. d. ges. Physiol. **197:**270-287, 1922.

and scopolamine and possibly by atropine. Hinsey and McNattin [7] were unable to confirm the inhibitory action of scopolamine even with as large doses as 7 mg. Gasser and Dale [8] found a similar inhibition with 2 mg. of atropine. For this reason and because nicotine does not stimulate the parasympathetic nerves, Dale and Gasser [9] objected to the assumption that the reaction must be associated with stimulation of parasympathetic structures. These observers experimented with many drugs, most of which had an action like that of nicotine and muscarine, and found that many quaternary bases, at least, have an effect on denervated muscles resembling that of nicotine.

Dale and Gasser showed the inhibitory effect of nicotine to direct stimulation of the denervated muscle and corroborated [8] the inhibitory action of epinephrine to a subsequent injection of acetylcholine. Finally, Hinsey and Gasser [10] demonstrated, in addition, that epinephrine prevents the Sherrington phenomenon produced by stimulation of the divided sciatic nerve. Gasser and Dale came to the conclusion that denervation sensitizes the mammalian cross-striated muscle and conveys to it properties which normally are part of the avian muscle.

EXPERIMENTAL DATA

In the following experiments sixteen cats were used. The weight of the animals varied from 3 to 4 Kg. The third nerve was sectioned intracranially with the use of sodium amytal anesthesia, and the animal was allowed to recover. At the time of operation immediate dilatation of the ipsilateral pupil showed that the section of the third nerve had been successful. After the cat had fully recovered from the anesthesia, further evidence of paralysis of the third nerve, in addition to the dilated pupil, was slight but definite narrowing of the palpebral fissure and immobility of the eyeball except in lateral deviation, as seen by turning the cat's head. From seven to forty-two days after section of the third nerve intracranially, the cat, under sodium amytal anesthesia, was subjected to a series of experiments, the results of which either were photographed by means of a motion picture camera or were recorded on a kymograph by means of an aluminum lever attached to the eyelid. The power of the tarsal muscle was insufficient to bring into action even our lightest tension lever.

Effect of Acetylcholine.—From 1 to 2 mg. of acetylcholine was injected into the ipsilateral carotid artery. Before completion of the injection, the ipsilateral palpebral fissure dilated, and the nictitating membrane retracted. The widening

7. Hinsey, J. C., and McNattin, R. F.: Further Observations on the Sherrington Phenomenon, Anat. Rec. **42**:50-51, 1929.

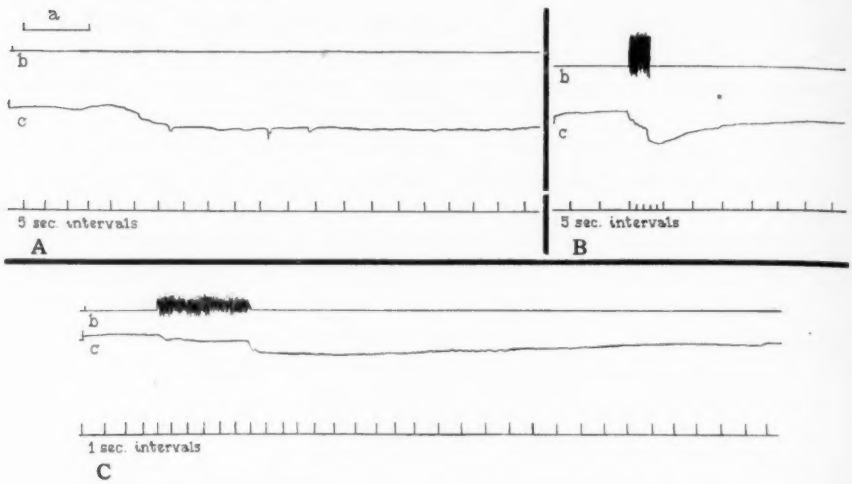
8. Gasser, H. S., and Dale, H. H.: The Pharmacology of Denervated Mammalian Muscle: II. Some Phenomena of Antagonism, and Formation of Lactic Acid in Chemical Contracture, J. Pharmacol. & Exper. Therap. **28**:287-315, 1926.

9. Dale, H. H., and Gasser, H. S.: The Pharmacology of Denervated Mammalian Muscle: I. The Nature of the Substances Producing Contracture, J. Pharmacol. & Exper. Therap. **29**:53-67, 1926.

10. Hinsey, J. C., and Gasser, H. S.: The Sherrington Phenomenon, Am. J. Physiol. **87**:368-380, 1928.

of the palpebral fissure was a very slow reaction of the upper and lower lids, reaching maximal dilatation in approximately fifteen seconds, and was followed by slow narrowing of the fissure, requiring thirty or more seconds to return to normal (fig. *A*).

A second injection before complete recovery had taken place failed to cause repetition of the reaction.



The tracings are taken from kymographic records. *a* indicates the time of injection; *b*, the period of faradic stimulation, and *c*, the movement of the upper eyelid. The movement of the eyelid was recorded by means of a long, light aluminum lever with a counterweight, attached to the upper eyelids on the side of the sectioned third nerve. A downward movement on the record indicates an upward movement of the eyelid. The ratio of movement of the eyelid to the degree of movement recorded is 1 : 4.

A shows the effect of injection of acetylcholine into the ipsilateral common carotid artery. The injection took fifteen seconds, indicated by *a* in the graph. After an initial slight narrowing of the palpebral fissure for from five to six seconds, slow widening of the fissure was observed during a period of twenty-three seconds. The upper eyelid moved 1.75 mm. This enlargement lasted fifty seconds, and then the eyelids returned to the original position.

B shows the effect of faradic stimulation of the peripheral stump of the first division of the trigeminal nerve on the side of the ptosis.

During stimulation there was slow widening of 1.25 mm. for three seconds; after stimulation, faster widening at 1.25 mm. for one-fifth second, and again slow widening of 1 mm. for two seconds. The total enlargement was 3.5 mm., and there was return to the original position in thirty seconds.

C shows the effect of faradic stimulation of the peripheral stump of the first division of the trigeminal nerve on the side of the ptosis. The drum was moving more slowly in this tracing, as can be seen by the time markings of one second, allowing more detail of the movement.

During stimulation there was slow widening of 1.25 mm. for six seconds; after stimulation faster widening of 0.75 mm. for one and a half seconds, and again slow widening of 0.5 mm. for five seconds.

The total enlargement was 2.5 mm., and there was return to the original position in twenty-five seconds.

In one cat 5 mg. of acetylcholine failed to produce any reaction. At autopsy it was observed that the third nerve had not been completely divided.

Electrical stimulation of the ipsilateral levator palpebrae muscle during the effect of the reaction to acetylcholine failed to produce any response.

Effect of Nicotine.—Small doses were ineffective. After adequate doses (from 2 to 3 mg.) of nicotine were injected into the ipsilateral carotid artery, a reaction similar to that caused by acetylcholine, but not as marked, was produced. The ipsilateral pupil was enlarged and the corresponding palpebral fissure was widened slightly; the nictitating membrane became hyperemic and protruded at times after primary retraction.

Direct faradic stimulation of the levator palpebrae muscle on the affected side by means of the Harvard inductorium, at a coil distance of 8 cm., produced a minimal, slow, wormlike contraction after injection of nicotine. Direct stimulation of the levator muscle on the normal side caused a prompt, rapid movement with a coil distance of 11.5 cm.

Enlargement of the Palpebral Fissures with Application of Drugs After Unilateral Section of the Oculomotor Nerve

Drug	Amount Given, Mg.	Ipsilateral Fissure	Contralateral Fissure
Acetylcholine	1, intra-arterially	+++	—
Nicotine	2, intra-arterially	++	—
Epinephrine hydrochloride	1, intravenously	++++	++++
Atropine sulfate	1, intravenously	—	—
	Duration of Action		
Acetylcholine after epinephrine hydrochloride	20 min.	—	—
Acetylcholine after atropine sulfate	20 min.	+	—

Effect of Epinephrine and Atropine.—Injections of 1 cc. of a 1:1,000 solution of epinephrine hydrochloride into the femoral vein caused marked widening of both palpebral fissures and retraction of the nictitating membrane. Both eyes watered profusely, and the animal showed a marked general reaction.

Atropine sulfate, on the other hand, in doses of 1 mg. caused no marked widening of both palpebral fissures, dilatation of both pupils and retraction of the nictitating membrane (table).

Effect of Electrical Stimulation of the Peripheral Stump of the Previously Sectioned Third Nerve.—No reaction was produced in the animals by stimulation of the peripheral stump, regardless of the strength of the current, whether seven or forty-two days after section of the third nerve.

Effect of Stimulation of the Gasserian Ganglion and Its Three Divisions.—The Harvard inductorium was used in these experiments. Both electrodes were applied to the point of stimulation, in order to give maximal local effect.

Electrical stimulation of the gasserian ganglion with the root and its branches intact produced slight widening of the ipsilateral fissure and retraction of the nictitating membrane, but currents of sufficient strength could not be applied because of the marked general pain reaction.

After section of the posterior root of the fifth nerve and stimulation of the ganglion, more marked and definite widening of the ipsilateral palpebral fissure occurred. Stimulation of the ganglion, after section of the third division or of the second and third divisions, in each instance produced widening of the ipsilateral

palpebral fissure. After section of the first division stimulation of the ganglion became ineffective, while stimulation of the peripheral stump of the first division, but not of the second or third division, still produced the phenomenon (fig. *B* and *C*). A stimulus lasting from two to four seconds, with a coil distance of from 9 to 7 cm., was sufficient. The muscular contraction began during the stimulation and increased slowly. After cessation of the stimulus a new contraction set in, continued for approximately four seconds and gradually returned to normal in about one and one-half minutes. About one third of the effect occurred during stimulation, and two-thirds, after cessation of the stimulation. During stimulation, the nictitating membrane first protruded and then retracted.

Effect of Epinephrine and Atropine on the Phenomenon Produced by Electrical Stimulation of the Peripheral Stump of the Fifth Nerve.—Epinephrine inhibited the movement of the eyelid produced by electrical stimulation of the first division of the fifth nerve, in some animals up to twenty minutes. In others the phenomenon occurred in spite of the action of epinephrine. The variability of the action of epinephrine has been pointed out by other workers, and these results confirm their findings. Atropine, on the other hand, did not influence the reaction in any way; thus, the phenomenon occurred no matter how large the amount of atropine given.

Effect of Section of the Cervical Portion of the Sympathetic Trunk on the Phenomenon Produced by Chemical and Electrical Stimulation.—In these animals, simultaneously with the division of the oculomotor nerve the ipsilateral cervical portion of the sympathetic trunk was resected for about 1 cm. below the superior cervical ganglion. Subsequent injection of both acetylcholine and atropine enlarged the palpebral fissure and the pupil, as it did before cutting the cervical portion of the sympathetic trunk. Intravenous injection of from 5 to 10 mg. of ergotoxine increased the elevation of the upper eyelid, but no further dilatation of the palpebral fissure could be obtained by subsequent electrical stimulation of the gasserian ganglion or of the first division of the trigeminal nerve.

COMMENT

The results of the experiments described show that from seven to forty-two days after intracranial section of the oculomotor nerve in cats, intra-arterial injection of acetylcholine causes widening of the palpebral fissure on the side of operation. However, one effective dose of acetylcholine renders the muscle refractory for the time of its action to a second dose of acetylcholine as well as to direct electric stimulation (Dale and Gasser [9]). The same reaction, to a less marked degree, is produced by intra-arterial injections of nicotine. Epinephrine produces an entirely different effect. Both palpebral fissures enlarge, and there are marked dilatation of the pupils and general systemic effects.

Faradic stimulation of the peripheral stump of the first division of the fifth nerve, but not of the second or the third division, causes a reaction exactly similar to the injection of acetylcholine into the ipsilateral carotid artery. Epinephrine inhibited this reaction in some cats, while in others no effect was noted. Atropine did not inhibit the reaction, regardless of the size of the dose.

As in the experiments of Dale and Gasser,[9] direct faradic stimulation of the levator muscle of the affected side was ineffective during the action of nicotine and acetylcholine. The accompanying table gives a summary of the action of the different drugs on the denervated levator palpebrae muscle.

CONCLUSIONS

The conclusion may be drawn from these data that, in analogy with Vulpian's tongue phenomenon and with Heidenhain's lip phenomenon, a pseudomotor eyelid phenomenon can be elicited which follows exactly the premises established for these phenomena. The autonomic fibers mediating the movements of the eyelid described run to the periphery in the first division of the fifth nerve, while the autonomic fibers for the tongue phenomenon pass over the third division of this nerve.

The nature of these autonomic fibers cannot be defined in detail. The fact that destruction of the cervical portion of the sympathetic trunks did not prevent the action of either acetylcholine or epinephrine was not unexpected and did not exclude the possibility that the fibers in question are of sympathetic nature. Lewandowsky,[11] Langley[12] and Elliott[13] long ago showed that injection of epinephine after degeneration of the sympathetic fibers is fully effective in its action on the heart (Rothlin[14]), and on the pupil (Hess[15]). It remains open to discussion whether ergotamine prevents the effect of electric stimulation or whether it enlarged the palpebral fissure to such a degree that further dilatation may have been physically impossible.

Hinsey and Gasser[10] stated that the presence or absence of the sympathetic fibers is of no significance in the Sherrington phenomenon, and van Rijnberk[16] proved it experimentally.

It will be the purpose of a subsequent paper to show the intramedullary origin of the centrifugal autonomic fibers in the peripheral divisions of the fifth nerve and to discuss the mutual relations between the eyelid phenomenon and the tongue and lip phenomena.

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11. Lewandowsky, M.: Ueber die Wirkung des Nebennierenextraktes auf das Auge, Zentralbl. f. Physiol. **12**:599, 1898.

12. Langley, J. N.: Observations on the Physiologic Action of Extracts of the Supra-Renal Bodies, J. Physiol. **27**:237-256, 1901.

13. Elliott, T. R.: The Innervation of the Bladder and Urethra, J. Physiol. **35**:368-445, 1906.

14. Rothlin, E.: Recherches expérimentales sur l'ergotamine alcaloïde spécifique de l'ergot de seigle, Arch. internat. de pharmacodyn. et de thérap. **27**:459-479, 1923.

15. Hess, W. R.: Die Wirkung von Ergotamin auf das Auge, Klin. Monatsbl. f. Augenh. **75**:295-300, 1925.

16. van Rijnberk, G.: Recherches sur le tonus musculaire et son innervation, Arch. néerl. d. physiol. **1**:262-270, 1916-1917.

DISCUSSION

DR. STANLEY COBB, Boston: This phenomenon interests me especially; it recalls work I did several years ago and reported in collaboration with Dr. Mixter, our observation being on the third division of the trigeminal nerve. I should like to ask about the actual origin of the autonomic innervation of the levator palpebrae muscle. I believe that Dr. Grant has evidence of a pseudomotor phenomenon, and this indicates that there is in the muscle a substance that resembles acetylcholine, arising from autonomic innervation. I wish to ask if I am right in understanding that in operations on these patients the phenomenon disappeared on sectioning the motor root of the fifth nerve.

DR. H. G. WOLFF, New York: I should like to ask whether stimulation of the first division of the fifth nerve caused the effect described when the superior cervical sympathetic ganglion had been removed, it being assumed, of course, that the third nerve had been cut.

DR. WILDER PENFIELD, Montreal, Canada: Certainly some of the parasympathetic nerve supply must pass along the great superficial petrosal nerve, which crosses the field of operation and is often cut at the time of section of the fifth nerve. I suggest that it may be a question not altogether of section of the fifth nerve but of interruption of the great superficial petrosal nerve. This nerve carries fibers which are parasympathetic, at least as far as fibers for the secretion of tears and those to the mucosa of a part of the nasal passages are concerned. I do not know whether the nerve has to do also with the muscle which raises the eyelid.

DR. TRACY J. PUTNAM, Boston: I should like to ask Dr. Grant and Dr. Groff whether the time relations were similar in the experiments on animals and in the patients observed clinically, that is, whether there were any latent period and prolonged contraction of the eyelid and whether the time during which it contracted was approximately the same in the two instances. It seems to me that this is interesting because if the delayed prolonged contraction is duplicated in the patients, it might almost be regarded as myotonia atrophica in miniature. The muscle concerned in this phenomenon is slightly paretic and responds with an extended myotonic contraction, presumably to a parasympathetic stimulus. I should like to recall the experiments which Dr. Soma Weiss and Dr. Foster Kennedy did many years ago in work on myotonia, showing that myotonic muscles act in exactly this way, at least with regard to epinephrine and atropine. There now is evidence that acetylcholine precipitates myotonia in muscles which are not obviously myotonic on ordinary examination.

DR. F. H. LEWY, Philadelphia: I wish first to answer Dr. Putnam's question. As long as we did not compare accurately the movements in the patients and those in the cats, we were convinced that the movement in man was rapid, but when we compared the movements, we found it was fairly slow in man. Whether it is as slow as in the cat we cannot say.

Dr. Penfield's question, as far as I understand it, concerns the intermingling of all these nerves in the peripheral part of the course, and in regard to this I am not able to answer. We have had no experience in this direction. We are able to answer tentatively Dr. Cobb's question concerning the origin of these autonomic fibers. Certain data in the literature seem to indicate that the mesencephalic nucleus of the fifth nerve, with its very large cells, may have to do with autonomic innervation. We prepared, therefore, a series of animals, the data on which is not included in our motion-picture study, in which we divided the oculomotor nerve exactly as in the previous experiments and, in addition, the facial and the hypoglossal nerve. Two weeks after this operation we stimulated the mesencephalic

nucleus. On stimulating the most cephalic part of this nucleus on the side of the divided oculomotor nerve we could produce the same phenomenon in the eyelid as in the preceding experiments, possibly even more beautifully, just as was seen in stimulation of the gasserian ganglion. We did not get any reaction in the muscles of the face or tongue when this portion of the nucleus was stimulated. However, on stimulating the caudal end of the mesencephalic nucleus of the fifth nerve we obtained no reaction in the eyelid, but a very marked tongue phenomenon occurred, as described by Philipeaux and Vulpian. The tongue arched, touching the palate, especially in its posterior third; it became everted and thick and, after repetitive stimulation, hemorrhagic, but only on the ipsilateral side. This experiment shows that the mesencephalic nucleus is in some way connected with these autonomic pseudomotor phenomena and that there is also a topical arrangement within this nucleus. I should like to state that all these stimulations of the nucleus were ineffective after sectioning peripherally the divisions of the fifth nerve.

Much more troublesome is Dr. Wolff's question. We removed the superior cervical ganglion in the cat. Two weeks after this operation we found that the results of electrical stimulation and the reactions to drugs were the same as before the section of the sympathetic nerve. But we believe that this was not conclusive proof, as we are aware that the sympathetic ganglion cells of the carotid artery were not affected by cutting the sympathetic chain in the neck. We injected, therefore, into the same animal 10 mg. of ergotoxine, and after this injection all reactions were abolished. This seems to prove that the phenomenon is a sympathetic reaction and is in accordance with Hinsey's experiments on blood vessels in the spinal cord.

However, in the literature we found especially interesting data recorded by Rothlin. He stressed that drugs similar to ergotoxine in their action are entirely dependent on the previous condition of the tissue. He was able to produce with each drug either an effect or its opposite effect, depending on how he had previously treated the animal.

I believe, therefore, that one is not entitled to decide on the basis of pharmacologic experiment whether these fibers are sympathetic or parasympathetic. That was the reason that we confined ourselves to the term autonomic fibers.

EVIDENCES OF VASCULAR OCCLUSION IN MULTIPLE SCLEROSIS AND "ENCEPHALOMYELITIS"

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Recent experimental work [1] has made it seem probable that the lesions of multiple sclerosis and also those of the forms of "disseminated encephalomyelitis" which seem to represent a more acute stage of the same process [2] are produced by a local circulatory disturbance, apparently of the nature of an obstruction on the venous side. According to this point of view, there must be a primary change in the contents of the vessels of the central nervous system, or possibly of the intimal lining, which leads to thrombosis of venules. This produces local passive congestion and a mild degenerative process which affects myelin sheaths more than other structures. The myelin degenerates and is phagocytosed. The "inflammatory" phenomena would then be regarded as secondary or symptomatic and the gliosis as reparative or reactive. This hypothesis obviously must remain largely a speculation as long as it rests on the results of experimentation with animals alone. The object of this paper is to present evidence from human pathologic material bearing on the question.

While many authors have described the condition of the vessels in multiple sclerosis, chief attention has been paid to perivascular infiltration and adventitial proliferation. It is perhaps worth while to emphasize the fact that the changes in the adventitia must be secondary to the cause of the lesion, whatever that may be assumed to be, and on that account they will receive only passing mention here. The point at issue

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This is the ninth of a series of investigations on multiple sclerosis.

Read at the meeting of the Boston Society of Psychiatry and Neurology, Feb. 20, 1936.

From the department of neurology, the Harvard University Medical School, and the Neurological Unit, the Boston City Hospital.

The expenses of this investigation were defrayed by the multiple sclerosis fund of Harvard University.

1. (*a*) Putnam, T. J.; McKenna, J. B., and Morrison, L. R.: Studies in Multiple Sclerosis: I. The Histogenesis of Experimental Sclerotic Plaques and Their Relation to Multiple Sclerosis, J. A. M. A. **97**:1591 (Nov. 28) 1931. (*b*) Putnam, T. J.: Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, Arch. Neurol. & Psychiat. **33**:929 (May) 1935.

2. Putnam, T. J.: Studies in Multiple Sclerosis: VII. Similarities Between Some Forms of "Encephalomyelitis" and Multiple Sclerosis, Arch. Neurol. & Psychiat. **35**:1289 (June) 1936.

is whether the structural changes observable in the bed of the blood stream are compatible with the conception of a primary vascular occlusion or congestion.

HISTORICAL REVIEW

Vascular Abnormalities in Multiple Sclerosis.—The list of authors who have reported observations of thrombi, obliteration, proliferation and engorgement of vessels and perivascular hemorrhages in cases of multiple sclerosis, as given by Borst [3] and extended by Dawson [4] and Jakob,[5] is of impressive length. It begins with the pioneers: Cruveilhier (1839) compared the areas of sclerosis with the results of embolism; Rindfleisch (1863) pointed out the presence of an engorged vessel in the center of smaller plaques, and Charcot (1863) described vascular obstruction. There is perhaps no need to reproduce the whole list here, as in most instances the observation was made in passing, without adequate description or illustration.

A few pathologists have devoted particular attention to the presence of thrombi. Of these, the earliest was Ribbert,[6] who not only described numerous thrombi composed of white cells and fibrin in arteries but gave an illustration. Neither the description nor the drawing can be said to be convincing. Williamson [7] also laid great emphasis on the presence of venous thrombi but did not describe them in detail. Borst [3] described fresh thrombi with softenings, and even destruction of the wall of the vessel in one of his cases and a calcified thrombus in another.

Other observers, for example Taylor,[8] have made a specific search for thrombi, without seeing them. Dawson, in his unparalleled monograph [4] (page 650), remarked:

> During the course of this investigation, a large number of small isolated areas, both in the brain and spinal cord, have been cut in serial section with the object of tracing the possible presence of thrombosis or of capillary hemorrhages. In a few instances, especially in the lateral vessels of the cord and medulla, there have been found aggregations of white cells and the presence of fibrin which have been taken as evidence of intra-vital thrombosis, but nowhere has evidence been present of organization of such thrombi nor of alterations in the vessel walls in relation to

3. Borst: Die multiple Sklerose des Zentralnervensystems, Ergebn. d. allg. Path. u. path. Anat. **9**:67, 1903.

4. Dawson, J. W.: The Histology of Disseminated Sclerosis, Tr. Roy. Soc. Edinburgh **50**:517, 1916.

5. Jakob, A.: Normale und pathologische Anatomie und Histologie des Grosshirns, Vienna, Franz Deuticke, 1929, vol. 2, pt. 1, pp. 797-848.

6. Ribbert, H.: Ueber multiple Sklerose des Gehirns und Rückenmarks, Arch. f. path. Anat. **90**:243, 1882.

7. Williamson, J. W.: The Early Pathological Changes in Multiple Sclerosis, Manchester M. Chron. **9**:373, 1894.

8. Taylor, E. W.: Zur pathologischen Anatomie der multiplen Sklerose, Deutsche Ztschr. f. Nervenh. **5**:1, 1894.

them, nor have these always been in relation to sclerotic areas. . . . It was impossible to trace, except in rare instances, a primary proliferation of the capillary endothelium.

Hassin [9] wrote:

Some areas, especially in the cortex, showed a greater wealth of capillaries, but no signs of budding, no regressive changes (such as hyaline degeneration, for instance), no marked thrombi formation, and only exceptionally—inflammatory cells (lymphocytes, plasma cells, polyblasts, etc.). Nor were hemorrhages with reactive phenomena found, though occasionally pigment was present within macrophages found around smaller capillaries.

In an extensive survey of the literature over many years, I have been unable to find any description of the organization of a thrombus in progress in a case of multiple sclerosis.

Obliteration of vessels has been recorded far more frequently than the presence of fresh thrombi, but no real descriptions or illustrations are available. Thus, Borst,[3] who founded a theory on the occurrence of vascular obstruction, gave no further description of the process than "significant narrowing of the lumen to the point of complete obliteration, hyaline transformation, etc." But he gave references to fifteen other authors who observed similar changes, which also have been recorded many times since.

It is admitted generally that the vessels may proliferate and appear to be engorged. Borst,[3] for example, described the dilatation and tortuosity of vessels in two cases with great vividness and remarked that new capillaries with proliferated endothelial lining may be observed in fresh plaques. He gave a large number of references. More recent authors have laid less stress on the engorgement, but it is well illustrated in three of Dawson's photographs [4] (figs. 445, 446 and 447). A sprouting capillary is shown in one of Dawson's drawings (fig. 12). On the other hand, plaques with a diminished blood supply have been described. The most definite account of this phenomenon is that given by Anton and Wohlwill.[10] In a case in which acute and chronic lesions existed at the same time, they observed in general the appearance of engorgement of vessels. In certain plaques, however, the number of capillaries containing blood was strikingly diminished when compared with similar areas in the "normal" tissue by means of careful counts and measurements. No one since appears to have taken as much trouble in determining the degree of congestion.

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9. Hassin, G.: The Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:589 (May) 1922.

10. Anton, G., and Wohlwill, F.: Multiple nicht eitrige Encephalomyelitis und multiple Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:31, 1912.

Perivascular hemorrhages have been described frequently. Siemerling and Raecke [11] laid particular emphasis on them. Dawson [4] regarded them as artefacts, but Borst [3] admitted their occurrence, which he related to the congestion of vessels. Borst also mentioned the presence of pigment, apparently hematogenous, and referred to a long list of older authors who had noted it. The presence of pigment was confirmed by Hassin.[9]

Vascular Abnormalities in "Encephalomyelitis" and Diffuse Sclerosis.—Since there are numerous parallels between multiple sclerosis and certain forms of "demyelinating encephalomyelitis," such as the postinfectious types,[2] the diffuse periaxial type,[12] *neuromyélite optique* [13] and dementia paralytica,[14] it may be pertinent to review briefly the endovascular changes in these diseases also.

Practically all authors who have described postvaccinal and postmeasles "encephalitis" since the reports of Barlow and Penrose (cited by Greenfield [15]) and Turnbull and McIntosh [16] have mentioned the extraordinary congestion which even in gross specimens is an unmistakable feature of the disease. The localization and appearance of the congestion have been well reviewed and described by Finley.[17] In some instances not only congestion but perivascular hemorrhage and deposits of pigment have been reported.[18] Indeed, the attempt has been made to establish a special hemorrhagic form of the disease—an attempt which is probably unjustified, as will be indicated later.

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11. Siemerling, E., and Raecke, U.: Zur pathologischen Anatomie und Pathogenese der multiplen Sklerose, Arch. f. Psychiat. **48**:824, 1911.

12. Wertham, F.: Small Foci of Demyelinization in the Cortex and Spinal Cord in Diffuse Sclerosis: Their Similarity to Those of Disseminated Sclerosis and Dementia Paralytica, Arch. Neurol. & Psychiat. **27**:1380 (June) 1932.

13. van Bogaert, L.: Erreur de diagnostique: Neuromyélite optique aiguë, premier stade d'une sclérose en plaques typique, J. de neurol. et de psychiat. **32**: 234, 1932.

14. Spielmeyer, W.: Ueber einige anatomische Aehnlichkeiten zwischen progressiver Paralyse und multipler Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **1**:660, 1910.

15. Greenfield, J. G.: The Pathology of Measles Encephalitis, Brain **52**:171, 1929.

16. Turnbull, H., and McIntosh, J.: Encephalomyelitis Following Vaccination, Brit. J. Exper. Path. **7**:181, 1926.

17. Finley, K.: Perivenous Changes in Acute Encephalitis Associated with Vaccination, Variola and Measles, Arch. Neurol. & Psychiat. **37**:505-514 (March) 1937.

18. Wohlwill, F.: Ueber Encephalomyelitis bei Masern, Ztschr. f. d. ges. Neurol. u. Psychiat. **112**:20, 1928. Greenfield.[15] Turnbull and McIntosh.[16]

The literature on the occurrence of thrombosis has been well reviewed by Kreider [19] and will be only briefly summarized here. Thrombi have been described by several authors.[20]

Diffuse sclerosis and the acute diseases which resemble it have been made the subject of an excellent monograph by Bouman.[21] He stated: "In nearly all cases the blood vessels inside the patch are proliferated. . . . In some cases there was swelling and proliferation of endothelial cells." Preagonal hemorrhages and deposits of blood pigment have been reported. I have been unable to find any description of thrombosis.

Bodechtel and Guttmann [22] in their article on diffuse sclerosis included two cases in which the lesions appeared to be secondary to the circulatory disturbances of congenital heart disease; yet the histologic changes simulated closely those in the other cases in the series.

The literature on the pathologic changes in *neuromyélite optique* is meager, but in at least one reported case a thrombus appeared to be responsible for one of the lesions.[23]

Dementia paralytica, taken as a whole, scarcely belongs in this group. In none of the forms of "encephalomyelitis" which I have listed is there such an intense meningitis, which in dementia paralytica is obviously of infectious origin. The mechanism of the degenerative changes in the cortex, and especially of those in the white matter, which so closely resemble sclerotic plaques, is more obscure. It has been suggested long since that the iron-containing pigment is derived from hemoglobin.[24] Work in progress in this laboratory appears to promise additional evidence that such is the case and, further, that the degenerative changes in the parenchyma are due to reduction of the capillary bed.

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19. Kreider, P.: Measles Encephalomyelopathy with Venous Thrombosis, to be published.

20. Lechelle, P.; Bertrand, I., and Fauvert, E.: Observation d'un cas d'encéphalite morbilleuse. Étude anatomique. Considérations étiologiques et pathologiques, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:898 (June 1) 1931. Ferraro, A., and Scheffer, I. H.: Encephalitis and Encpehalomyelitis in Measles: A Pathologic Report of Six Cases, Arch. Neurol. & Psychiat. **25**:748 (April) 1931. Hassin, G., and Geiger, J. C.: Postvaccinal (Cowpox) Encephaliltis: A Clinicopathologic Report of a Case, ibid. **23**:481 (March) 1930. Wohlwill.[18] Kreider.[19]

21. Bouman, L.: Diffuse Sclerosis: Encephalitis Periaxialis Diffusa, Bristol, John Wright & Sons, Ltd., 1934.

22. Bodechtel, G., and Guttmann, E.: Zur Pathologie und Klinik diffuser Markerkrankungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:544, 1932.

23. Cestan, Riser and Planques: De la neuro-myélite optique, Rev. neurol. **2**: 741, 1934.

24. Spatz, H.: Zur Eisenfrage, besonders bei der progressiven Paralyse, Zentralbl. f. d. ges. Neurol. u. Psychiat. **27**:171, 1921-1922.

Relation of Lesions to Vascular Territories.—Anton and Wohlwill,[10] Dawson [4] and Falkiewicz [25] studied the relationship between vascular territories and sclerotic plaques in serial sections. They all arrived at the same conclusion: that small plaques extend along the central vessel like a sleeve, following its branches and occasionally coalescing. It was not possible to demonstrate a coincidence between the plaque and the capillary territory of an artery (which, as will become evident later, is a variable area). Dawson found the central vessel to be always a vein, as is, of course, the usual situation in the "encephalomyelitides." Many older observers (for example, Rindfleisch [26]) called attention to the fact that a fresh plaque usually is bluish or grayish when first cut but becomes pinkish with exposure to the air. This suggests strongly that the dilated vessels contain venous blood.

Occurrence of Areas of Softening in Multiple Sclerosis and Its Significance.—The universally recognized, but not inevitable, result of vascular closure is an area of softening, that is, an area in which all nerve elements are destroyed and the loss of tissue is replaced by a cyst or mixed glial and mesodermal scar. If sclerotic plaques are due to vascular obstruction, such areas of softening should occur occasionally. As a matter of fact, they do. Areas of complete loss of nerve tissue—axis-cylinders and nerve cells, as well as myelin—have been reported by practically all histologists who have gone deeply into the subject (for example, Dawson [4] gave illustrations of complete loss of axis-cylinders [figs. 363, 364 and 366] and of almost complete loss of ganglion cells [fig. 419]). Actual fresh softenings and cyst formations in the course of multiple sclerosis have been reported by Cramer,[27] Borst,[3] Anton and Wohlwill,[10] von Weizsäcker,[28] Wohlwill [18] and others. In "encephalomyelitis" the lesions are often described as softenings, and in two instances (Walthard [29] and Herkenrath [30]) cyst formation was disclosed

25. Falkiewicz, T.: Zur Pathogenese der multiplen Sklerose, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **28**:172, 1926.

26. Rindfleisch: Histologische Detail zu der grauen Degeneration von Gehirn und Rückenmark, Arch. f. path. Anat. **26**:474, 1863.

27. Cramer, A.: Beginnende multiple Sklerose und akute Myelitis, Arch. f. Psychiat. **19**:667, 1888.

28. von Weizsäcker: Ein ungewöhnlicher perakut verlaufender Fall von multipler Sklerose mit anatomischem Befund, Monatschr. f. Psychiat. u. Neurol. **49**: 221, 1921.

29. Walthard, K. M.: Spätstadium einer "Encephalitis" nach Masern, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**:176, 1929.

30. Herkenrath, B.: Pathologisch-anatomisch gesicherte Ausheilung eines Falles von Encephalitis post vaccinationem, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:293, 1935.

at autopsy, after the acute stage had been passed. In Cramer's case of postmeasles "encephalitis," both sclerotic plaques and an acute area of "myelitis" were present. Further notes on this question will be found in a previous study.[2]

Recapitulation.—To sum up the observations of authorities who have committed themselves definitely in regard to the state of the vascular bed in lesions of multiple sclerosis and "encephalomyelitis": It may be said that the great majority have reported vascular abnormalities of one kind or another—thrombi, vascular occlusions, congestion, perivascular hemorrhage or the deposit of hematogenous pigment or some combination of these. Adequate descriptions and illustrations of the alterations are lacking, however, as far as I have been able to learn. Of the few authors who deny the existence of circulatory disturbances, some, at least, have not employed histologic technics adapted to the study of blood vessels and their contents. The presence of thrombi in the lesions of "encephalomyelitis" has been recorded frequently.

Vascular abnormalities have been stated to play a rôle in the etiology of the disease by several authors who have described them, but usually a secondary part, merely permitting the escape of toxins into the tissue. Williamson at one time [7] gave an interpretation of his observations similar to that suggested at the beginning of this paper, but he appears to have modified it later.[31] There has been a surprising dearth of attempts to confirm pathologic observations by experiment, or even by comparison with other conditions in which the mechanism is more obvious.

THEORETICAL CONSIDERATIONS: THE CEREBRAL CIRCULATION

Before proceeding to a description of the material and methods employed in the present investigation [3] it may be well to recall some facts, old and new, which have a bearing on the problem in hand. Recent studies by Pfeifer [32] and others have given a new and vivid conception of the anatomic features of the cerebral and the medullary blood supply. There are no true "end-arteries" in the old sense; on the contrary, there is a rich anastomosis of vessels, particularly among veins and capillaries but also among arteries. The extent of an arterial "territory" depends largely on the adequacy of the collateral circulation, while venous "territories" are even more diffuse. The capillary supply of the gray matter is far richer than that of the white and of a somewhat different pattern. There are peculiarities in the venous drainage.

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31. Williamson, R. T.: On the Etiology and Pathology of Disseminated Sclerosis, M. Chron. **4**:261, 1903.

32. Pfeifer, R.: Grundlegende Untersuchungen über die Angioarchitektonik des menschlichen Gehirns, Berlin, Julius Springer, 1930.

Rather small venules may pursue a long and tortuous course before opening suddenly into large trunks, which conduct the blood to the pial surface. Veins in the white matter appear to have some nutritive function, since crystalloids diffuse easily through their walls [33] and they are often surrounded by a zone relatively free from capillaries.[32]

Physiologically, also, the cerebral circulation has peculiarities. The blood flow is slow and the oxygen consumption high, so that the blood in the internal jugular vein has an unusually low oxygen content.[34] The oxygen consumption of the cortex is probably far greater than that of the white matter. Even histologically a chemical difference may be demonstrated: In sections from the nervous system fixed in formaldehyde and stained with acid fuchsin (Mallory's connective tissue stain) the corpuscles in the gray matter stain red, while those in the white do not.

HISTOLOGIC RESULTS OF VASCULAR OBSTRUCTION IN THE NERVOUS SYSTEM

The effects of disturbances of the arterial supply to the brain have been studied. Ligation of a sufficient proportion of the vessels to the brain results in widespread degeneration of the cortex, with inconspicuous changes in the white matter.[35] Small emboli introduced into the carotid artery under certain circumstances may produce no lesions.[1a] Cortical lesions are produced more commonly.[36]

Embolic lesions in the white matter are usually cystic, but certain embolic methods may produce a milder injury, affecting the myelin far more than the axis-cylinders.[1a]

Any of these changes may be observed as a result of the ordinary types of arteriosclerosis of the brain. It is a commonplace of neuropathology that such lesions may produce infiltration into the surrounding tissues, composed of lymphocytes and polycytes in the early stages, and may lead to local gliosis in the course of months. The degree of mesodermal proliferation is in general proportional to the mesodermal damage. Scars resulting from mild injuries may simulate closely sclerotic plaques, as has been emphasized by a recent study in this laboratory.[37]

33. Putnam, T. J., and Ask-Upmark, E.: The Cerebral Circulation: XXIX. Microscopic Observations on the Living Choroid Plexus and Ependyma of the Cat, Arch. Neurol. & Psychiat. **32**:72 (July) 1934.

34. Lennox, W. G.: The Constancy of the Cerebral Blood Flow, Arch. Neurol. & Psychiat. **36**:375 (Aug.) 1936.

35. Gildea, E., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

36. Bodechtel, G., and Müller, G.: Die geweblichen Veränderungen bei der experimentellen Gehirnembolie, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**:764, 1930.

37. Alexander, L.: Personal communication to the author concerning material in preparation.

The results of venous obstruction and congestion are far less well known. A recent experimental investigation,[1b] already alluded to, indicated that demyelinization is produced more readily by certain types of venous obstruction than is destruction of the gray matter. Studies in progress show that this is true also in human autopsy material and that histologic pictures closely simulating "encephalomyelitis" are common after venous thrombosis.[37] Cases of carbon monoxide poisoning,[38] of "chronic subcortical encephalitis"[39] obviously due to vascular disease and of diffuse sclerosis accompanying congenital heart disease, reported by Bodechtel and Guttmann,[22] might be interpreted in the same sense.

MATERIALS AND METHODS OF THE PRESENT STUDY

An assortment of blocks from seventeen cases of multiple sclerosis, contributed from various laboratories,[2] has formed the basis of several papers in this series. The duration of the disease varied from a few months to eighteen years. In seven cases the whole brain was available for study; in the remainder the material was limited. Cases were accepted for the group only after the histologic diagnosis of multiple sclerosis had been agreed on by at least two pathologists. In addition, histories typical of multiple sclerosis were available in most of the cases. "Encephalomyelitis" was represented by three cases in the collection of this laboratory—one of the postvaccinal type and two others in which the histologic picture was similar but the etiology unknown.

To demonstrate vascular changes various methods of fixation and staining were employed. The ordinary neuropathologic stains used as a routine proved almost useless. Proliferation of intima may be demonstrated with methylene blue and similar stains, but not fibrin, platelets or fibrosis. The hematoxylin and eosin stain gives a poor differentiation of the noncellular structures within vessels. The best results were obtained with Masson's connective tissue stain on thin paraffin sections of material fixed in solution of formaldehyde or Zenker's solution, and this was accepted as the standard method of study. It not only gives an exquisite differentiation of connective tissue, fibrin, red cells, serum and platelets but shows myelin, axis-cylinders and gliosis. Mallory's connective tissue stain and phosphotungstic acid and hematoxylin are also suitable for the purpose. The use of thin sections (12 microns or less) is essential for the study of vascular changes.

DEFINITION OF THROMBOSIS

It is not easy to predicate what does and what does not constitute a thrombus. Most descriptions in textbooks are based on the presence of clots adherent to the walls of large vessels and are not applicable to venules and arterioles. The statement is sometimes made that injury to the intima is essential as a first step in the formation of a clot. Recent

38. Meyer, A.: Experimentelle Erfahrungen über die Kohlenoxydvergiftung des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **112**:187, 1928.

39. Farnell, F., and Globus, J.: Chronic Progressive Vascular Subcortical Encephalopathy: Chronic Progressive Encephalitis of Binswanger, Arch. Neurol. & Psychiat. **27**:593 (March) 1932.

work has indicated that this is not the case and that the production of certain chemical changes in the blood may cause clotting in intact vessels.[40] Even in small vessels agglutination of platelets appears to be the primary change,[41] and any large accumulation of platelets may be accepted as the beginning of a clot in circulating blood, as they are so sparse that definite movement is necessary to allow a mass of them to form. This is not true of leukocytes, which have some motility and are often observed in groups in the cerebral vessels. Fibrin may or may not be present. Long, straight needles of fibrin presumably have formed after death. Antemortem fibrinous clots may be recognized

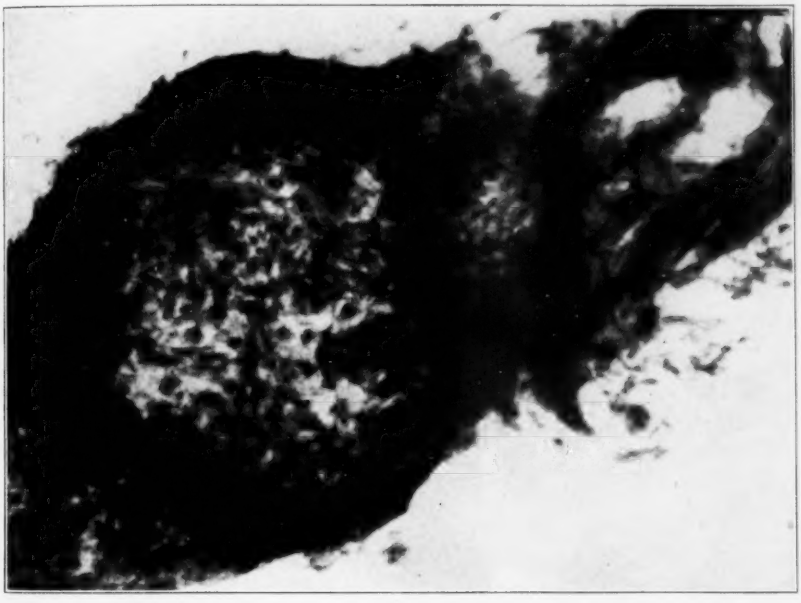

Fig. 1.—"Disseminated encephalomyelitis." Masses of agglutinated platelets are contained in a vessel from the vicinity of a patch of degeneration in the cerebral white matter. Masson stain.

sometimes by the fact that the strands of fibrin are heavy and curved toward the wall of the vessel, which is distended by the congestion proximal to the obstruction to the blood flow.

Clots of agglutinated red cells without fibrin strands doubtless occur also and are characterized by the fact that the individual cells are melted

40. Stuber, B., and Lang, K.: Die Physiologie und Pathologie der Blutgerinnung, Berlin, Urban & Schwarzenberg, 1930, pp. 74-78.

41. Johnson, W. R.: Experimental Thrombosis: The Appearance of Fibrin in the Early Stages of Formation of White Thrombus, Folia haemat. **48**:413, 1932.

together into an amorphous mass, which tends to fragment under the knife.[42] With all these criteria and with the knowledge that a clot must be present in a given section (e. g., in a vessel running into an abscess cavity), it may be impossible to demonstrate it.[37]

The subsequent development of a thrombus may be recognized more definitely. Within a few days, or less, organization begins. Endothelial cells swell, proliferate and fill the lumen. This stage of the process is equally brief. The vessel may then disintegrate entirely, leaving a

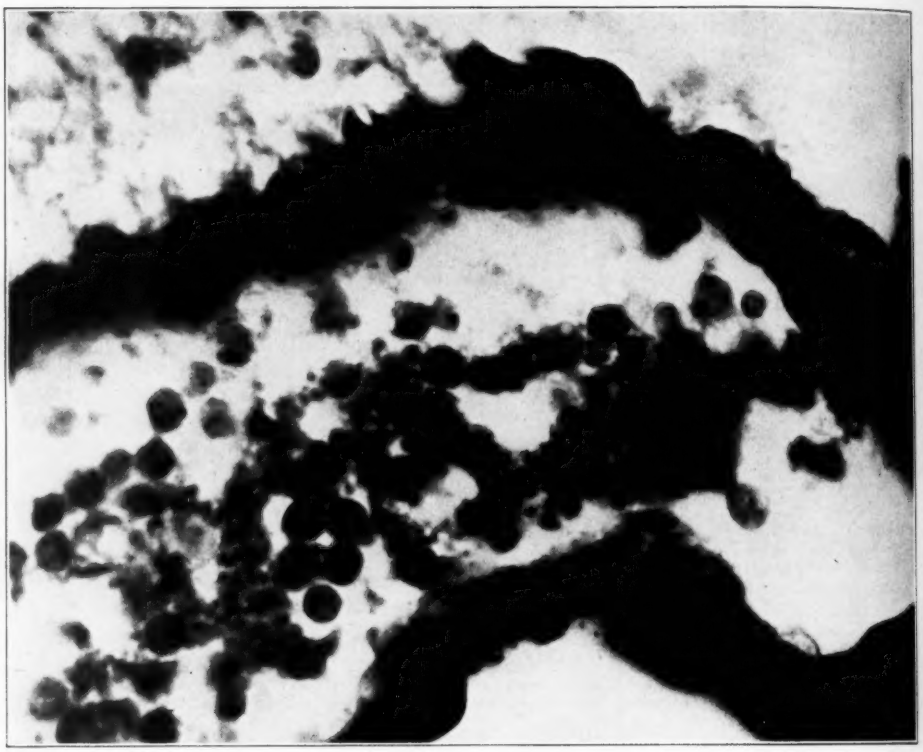

Fig. 2.—Multiple sclerosis. Agglutinated platelets are shown in a vein leading from a plaque. Mallory's connective tissue stain.

collection of fibers and leukocytes behind,[37] or the endothelial obstruction may become transformed gradually into a fibrous plug.

THROMBI IN "ENCEPHALOMYELITIS"

In all three cases of "encephalomyelitis" available for study numerous fresh thrombi were observed. The common type consisted of masses

42. Schmorl, G.: Die pathologisch-histologischen Untersuchungsmethoden, Leipzig, F. C. W. Vogel, 1925. Kreider.[19]

of agglutinated platelets (fig. 1) filling the lumen of the vessel. Occasionally the beginning of organization could be detected. An unusually heavy deposit of fibrin was present in many vessels.

THROMBI IN MULTIPLE SCLEROSIS

Definite thrombi were observed in veins in nine of the seventeen cases studied. The thrombus was not always in direct relation with a plaque, but Alexander [37] has shown that the tissue damage produced by

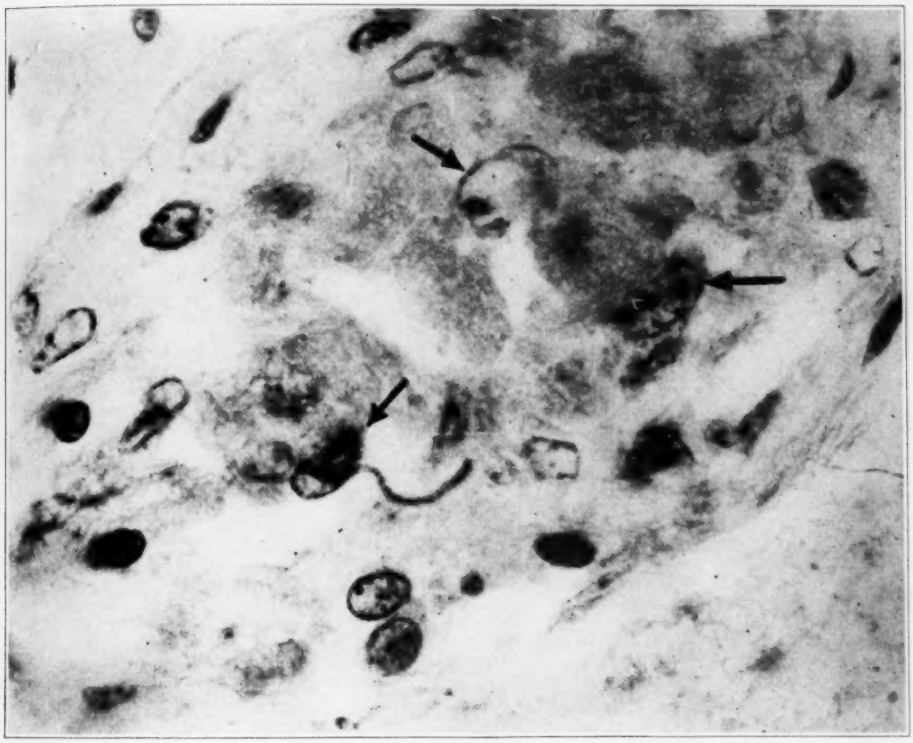

Fig. 3.—Multiple sclerosis. Arrows indicate endothelial cells invading clumps of platelets in a clot. Masson stain.

a venous obstruction often lies some distance proximal to the clot, so that the two are seldom encountered in the same section. When there was a lesion in the vicinity, it was invariably acute and devoid of gliosis, even when most of the plaques in the same brain were obviously old and sclerosed. The commonest type of thrombus, seen in eight cases, was an accumulation of platelets (fig. 2). In one case there were also mixed clots containing endothelial cells (fig. 3). In another instance

typical degeneration of the wall of the vessel had occurred (fig. 4). There was seldom much infiltration about the thrombosed vessel, and one could not say that the clot was secondary to local inflammation. The thrombi sometimes occurred in a single vessel in a section, but more often they appeared in groups. In one section practically all the vessels contained thrombi, in various stages of development. The use of serial sections aided materially in disclosing thrombosis of vessels in the vicinity of acute or advancing lesions.

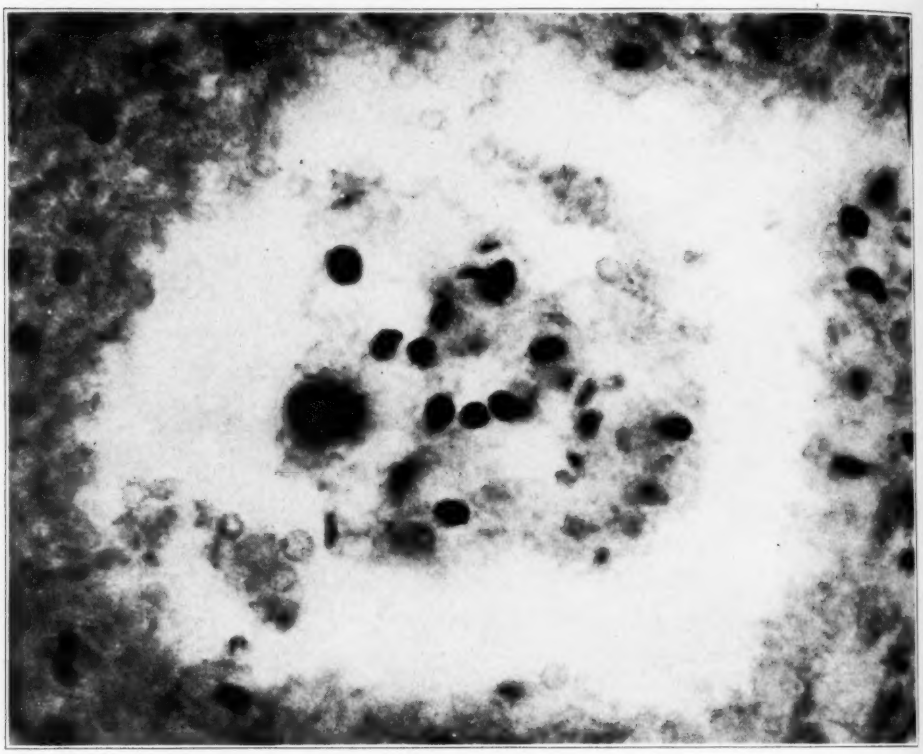

Fig. 4.—Multiple sclerosis. Disintegration of a small vessel is shown in a fresh plaque in the cerebral white matter. Hematoxylin and eosin stain.

CONGESTION AND PERIVASCULAR HEMORRHAGE IN "ENCEPHALOMYELITIS" AND MULTIPLE SCLEROSIS

Enormous dilatation of vessels and accumulation of pigment were seen in all three cases of "encephalomyelitis." In one, the case of the postvaccinal type, large perivascular hemorrhages occurring in relation to thrombosed vessels were observed in one block (fig. 5). In other blocks the usual perivascular demyelinization was observed.[2]

Engorgement and proliferation of vessels were also observed in many plaques of multiple sclerosis in eleven of the cases studied. In general, these processes appeared more intense in the more acute areas (fig. 6) and in those in which destruction of axis-cylinders as well as myelin had occurred.

Is the engorgement a result of a local inflammatory process; that is, is it active engorgement? To shed light on this point, a comparison was made between an acute congested plaque and the area of greatest congestion in the white matter in several cases of purulent meningitis without thrombosis of vessels (fig. 7). There could be no doubt that the vascularity was far greater in the acute plaque. The only case of

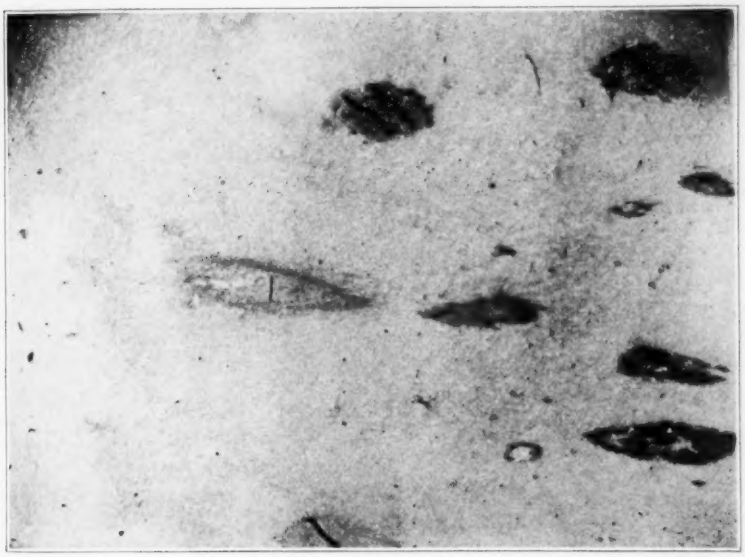

Fig. 5.—Postvaccinal "encephalomyelitis" with perivascular hemorrhages. The central vein usually contains a clot. Mallory's connective tissue stain.

meningitis in which there was congestion comparable to that of an acute plaque was one in which thrombosis of pial veins had extended into the white matter, and here demyelinization had occurred.[37]

Yellow pigment was observed about congested vessels in fifteen of the cases of multiple sclerosis (fig. 8), and occasionally within vessels (fig. 9). Alexander's micro-incineration studies[37] showed that this pigment contains iron and is therefore presumably hematogenous. Small perivascular hemorrhages were observed in most cases, some at least of which appeared to have occurred during life, since the cells had begun to break down or had been phagocytosed.

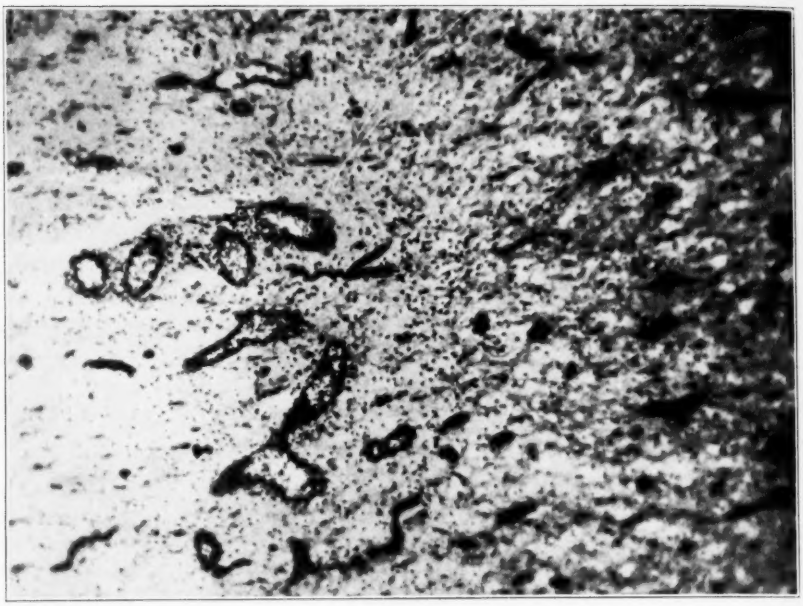

Fig. 6.—Multiple sclerosis. Engorgement of vessels is shown in a fresh plaque. Relatively normal white matter is seen to the right of the photograph. Masson stain.

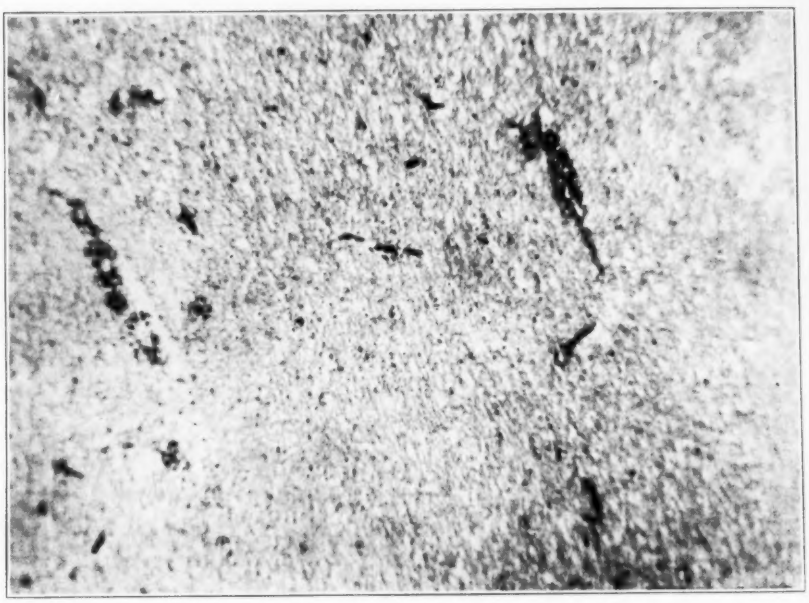

Fig. 7.—Streptococcic meningitis. This photomicrograph (same magnification as that in figure 6) represents an area of most intense congestion in a series of slides from several cases, showing that engorgement in a purely inflammatory disease is small compared to that in some plaques of multiple sclerosis. Masson stain.

OBLITERATION OF VESSELS IN MULTIPLE SCLEROSIS

Closure of vessels by fibrous plugs or endothelial cells was far more common than by thrombi. It was observed in fourteen cases. This is not surprising, for a thrombus is necessarily an evanescent structure, while a fibrous cord may persist indefinitely. Such cords are almost always to be seen in the large periventricular areas of sclerosis (fig. 10). Sometimes the endothelial cells persist, although no lumen can be discovered. In other instances only a single chain of connective tissue cells

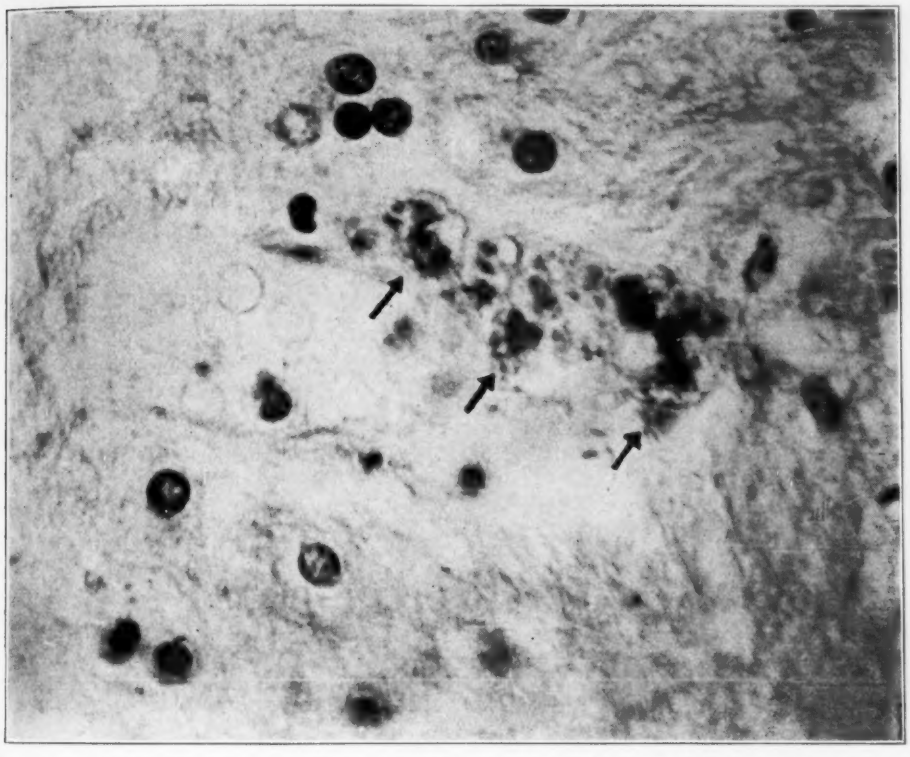

Fig. 8.—Multiple sclerosis. Arrows indicate a deposit of yellow pigment about a congested vessel. Masson stain; photographed with a green filter.

represents the remnant of the lumen of a vessel lying in the center of the persisting loose adventitia.

Is this closure the result of the perivascular infiltration? As a control, four cases of intense secondary degeneration about old apoplectic foci or areas of injury were studied. Vessels infiltrated with phagocytic and glia cells, so that the adventitia was greatly distended and thickened, were observed by means of the same stains as were used in the cases

of multiple sclerosis. In no instance was there any obstruction of the lumen of the vessel, nor were any fibrous cords observed. The vessels were on the whole far sparser than those in comparable sclerotic plaques.

AREAS OF COMPLETE PARENCHYMAL DESTRUCTION AND CYST FORMATION

As has already been recorded,[2] the majority of lesions in the cases studied showed a degree of destruction of axis-cylinders almost equal

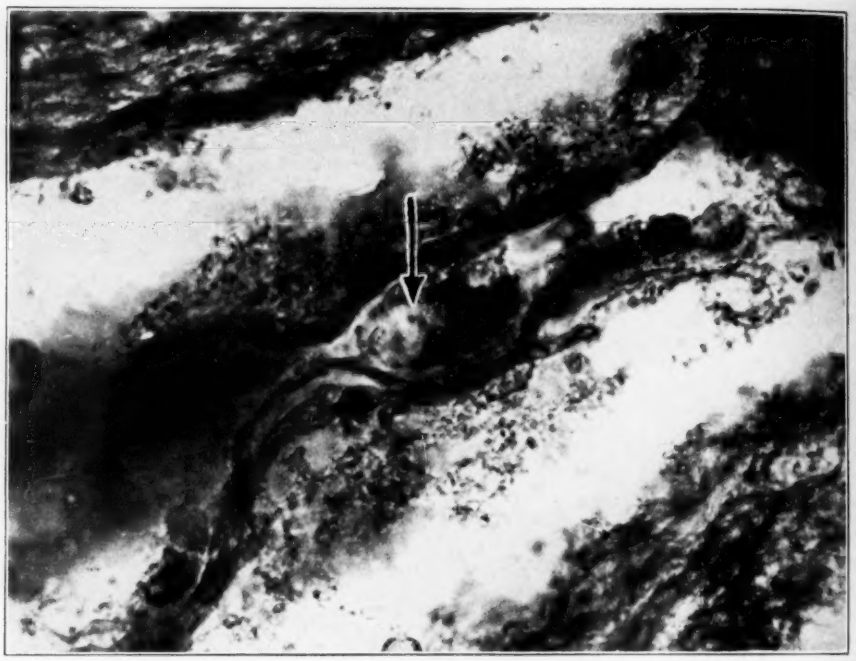

Fig. 9.—Multiple sclerosis. The arrow indicates yellow pigment within the lumen of the vessel. Masson stain.

to that of the loss of myelin. Focal necroses and "ischemic" changes in the ganglion cells were observed in the gray matter of the cord and cortex. In two cases there were definite small cysts of softening in the white matter (fig. 11). The more extreme types of injury and repair were comparable to those which have long been recognized as of ischemic origin.

LESIONS OUTSIDE THE NERVOUS SYSTEM IN MULTIPLE SCLEROSIS

The condition of the nonnervous organs in cases of multiple sclerosis has received little attention. If the disease is the result of vascular

occlusion—or, indeed, whatever its cause—evidence of a similar change might be expected elsewhere in the body.

Borst [3] insisted on the importance of examination of other organs but neglected to record it in his cases. He referred to three previous authors who had described fibrotic changes elsewhere in the body, but I have been unable to confirm his statement in the references given. Strümpell [43] stated that he had searched for vascular changes in the

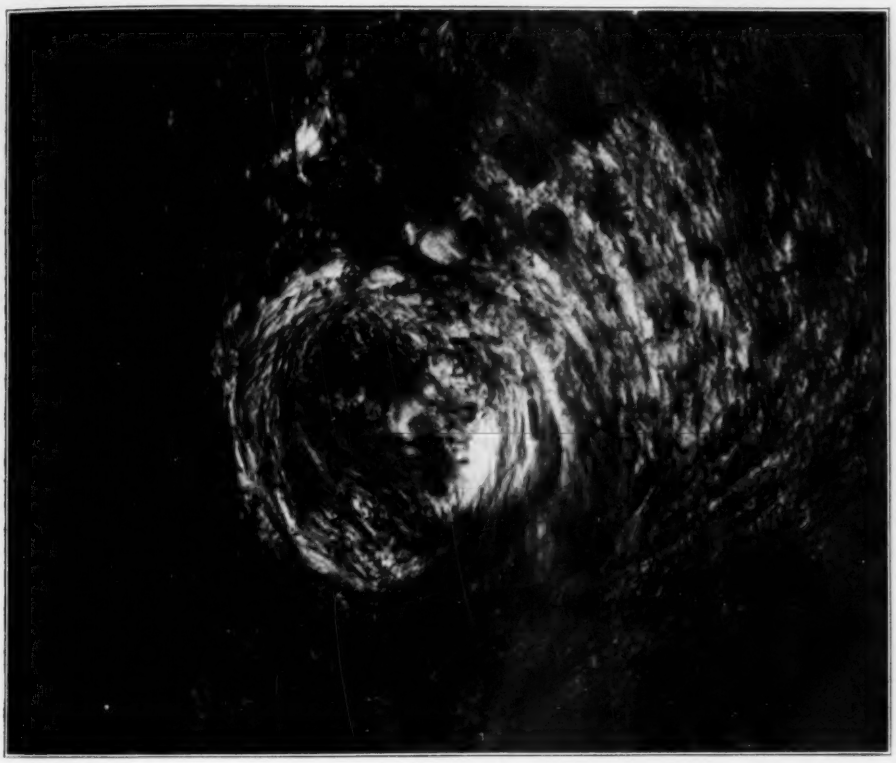

Fig. 10.—Multiple sclerosis. A vessel, in the vicinity of the lateral ventricle, is completely occluded by strands of connective tissue. Masson stain.

rest of the body but had failed to observe them. The problem has been ignored by recent writers.

Slides from the general autopsy were available for study in five of the cases of multiple sclerosis included in this series. One case was from the Peter Bent Brigham Hospital (Dr. S. B. Wolbach), one from the Boston State Hospital (Drs. N. Raskin and Leo Alexander) and

43. Strümpell, A.: Zur Pathologie der multiplen Sclerose, Neurol. Centralbl. **15**:961, 1896.

the other three from the Mallory Institute of Pathology of the Boston City Hospital (Dr. Frederic Parker Jr.).

The anatomic diagnoses were as follows:

CASE 1 (a woman aged 26).—The diagnosis was: multiple sclerosis; meningitis; bilateral cavernous sinus thrombosis, of infectious origin; bronchopneumonia; pulmonary thrombosis; abdominal adhesion; pyelitis; cystitis; abscesses of the kidney; edema of the legs; decubitus; hydrosalpinx; leiomyoma; cirrhosis of the liver, and focal necrosis.

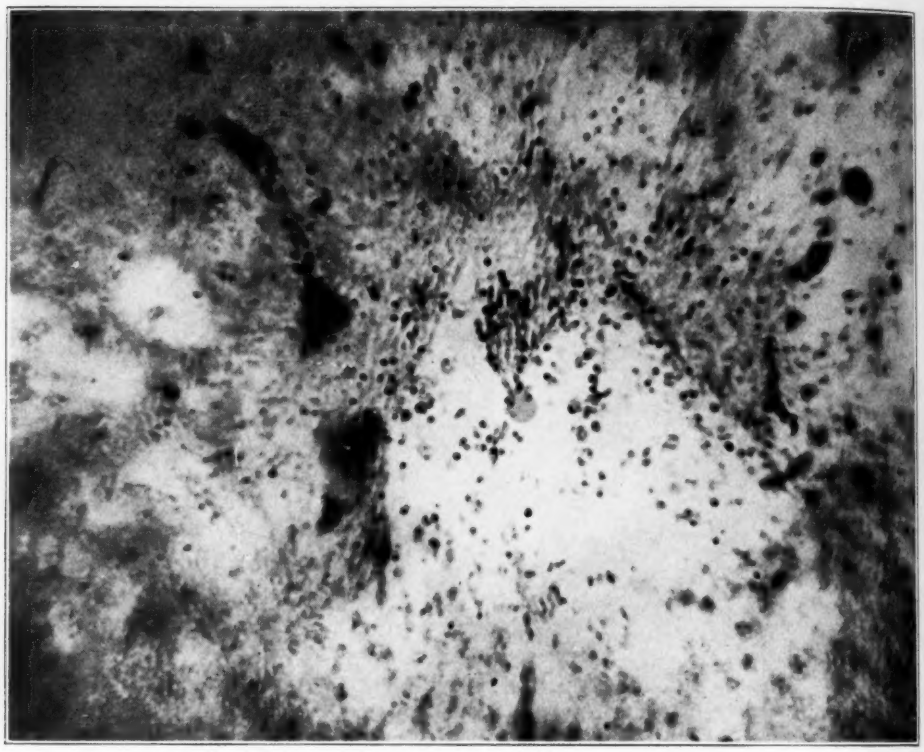

Fig. 11.—Multiple sclerosis. Small cysts of softening containing large phagocytes are seen in the cerebral white matter. Hematoxylin and eosin stain.

CASE 2 (a man aged 48).—The diagnosis was: multiple sclerosis; pericarditis; chronic pyelonephritis; renal calculus; acute splenic tumor, and cystitis.

CASE 3 (a man aged 46).—The diagnosis was: multiple sclerosis and bronchopneumonia.

CASE 4 (a woman aged 44).—The diagnosis was: multiple sclerosis; early bronchopneumonia; acute pleuritis; acute splenitis; acute pyelonephritis; chronic cystitis; chronic urethritis; endocervicitis, and decubitus ulcers.

CASE 5 (a woman aged 35).—The diagnosis was: multiple sclerosis; miliary tuberculosis of various organs; tuberculosis of the lungs, liver, adrenals, kidneys

and dura of the cervical portion of the cord; bronchopneumonia; cystitis, and pyelitis.

In all the cases the autopsy slides made as a routine were available for study. Fresh areas of infection in the lungs and kidneys complicated the study of these organs, but in each case there were swelling of the glomeruli and hyalinization of at least some of their tufts. Central necroses of the liver were present to a greater or less degree in all cases. There were mild fibrotic changes in the cardiac muscle. No other constant lesions were noticeable.

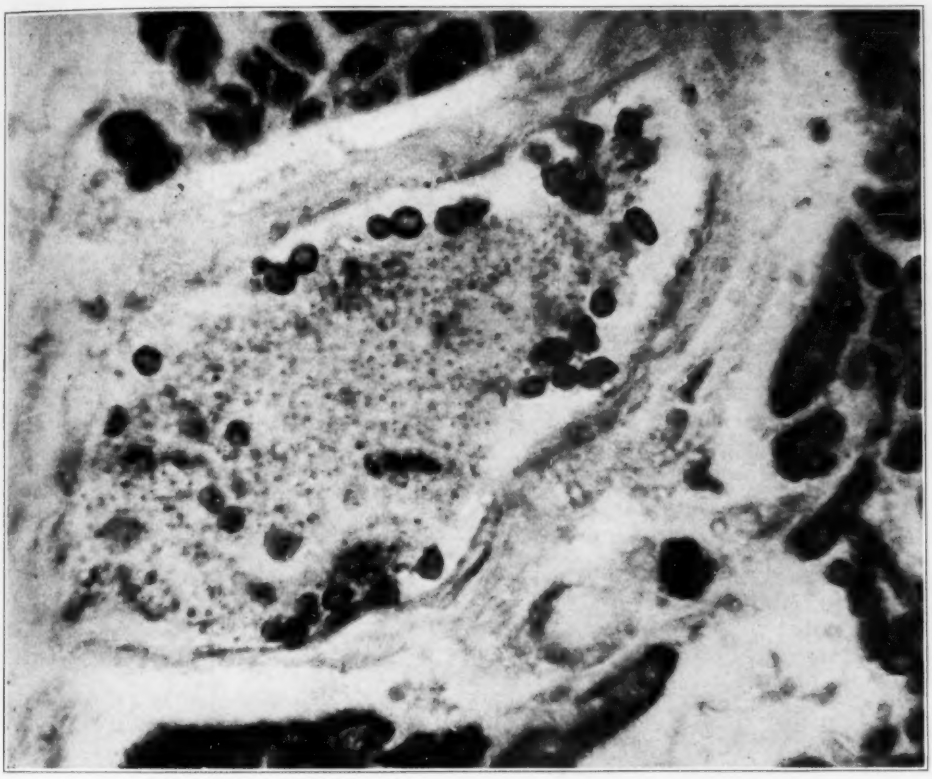

Fig.12.—Multiple sclerosis. A platelet thrombus is shown in a vessel in the cardiac muscle. Hematoxylin and eosin stain.

The cause of death in case 1 was thrombosis of the cavernous sinus. Microscopically, a platelet thrombus without reaction about it was observed in a vein of the cardiac muscle (fig. 12). In case 4 also a thrombus invaded by endothelial cells was present in the cardiac muscle (fig. 13). In case 5 a recently organized thrombus was present in a section from the heart, and there were several thrombi in the liver, some of which were in process of organization (fig. 14).

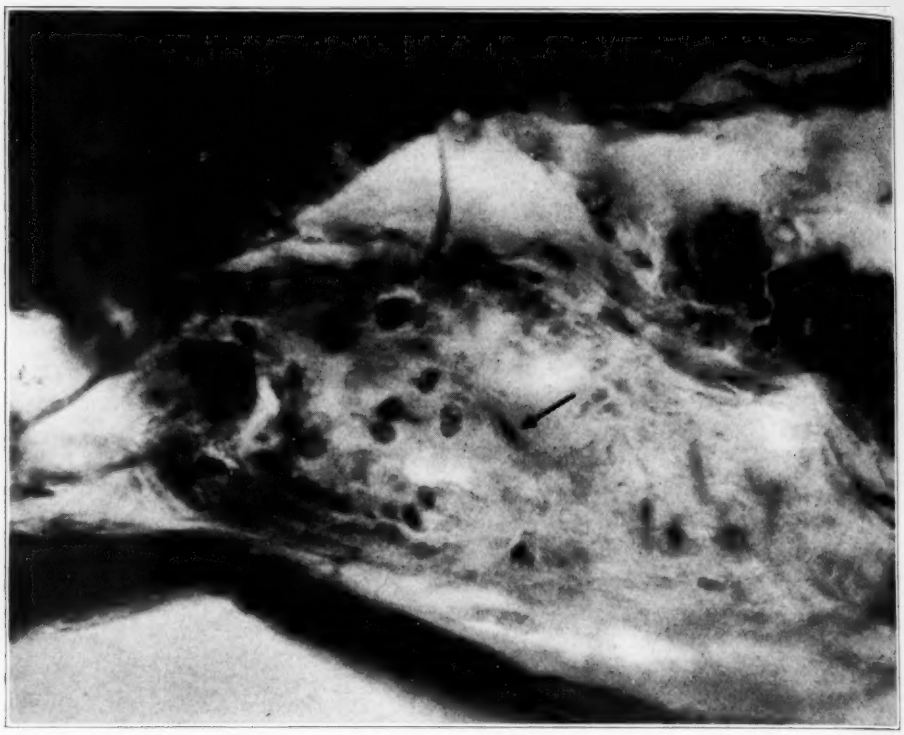

Fig. 13.—Multiple sclerosis. The arrow indicates endothelial cells invading a thrombus in the cardiac muscle. Masson stain.

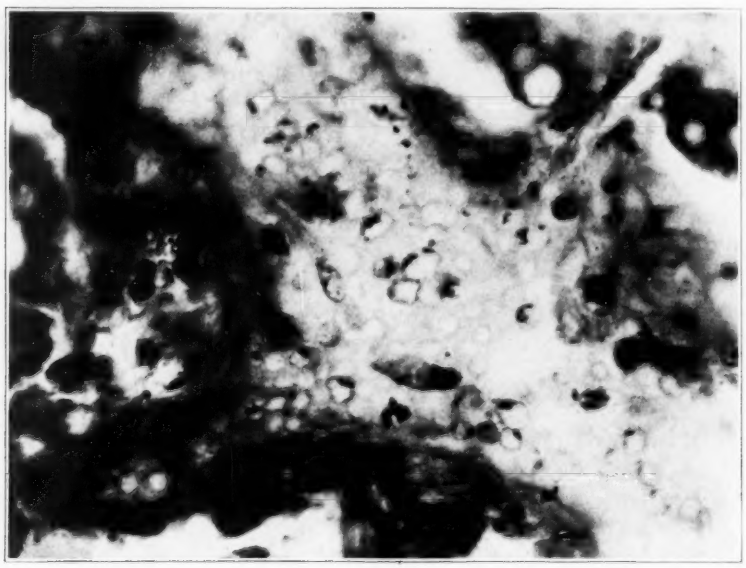

Fig. 14.—Multiple sclerosis. Endothelial cells are shown invading a thrombus in the liver.

In cases 1, 4 and 5 there were acute lesions also in the central nervous system, while in the other two cases the plaques consisted of sclerotic scars, with little congestion. Thus, one may say that casual inspection of slides made as a routine may reveal thrombi in organs other than the central nervous system, especially, perhaps, following exacerbations in cases of multiple sclerosis.

COMMENT

The present study has brought out strikingly the difficulties of recognizing vascular obstruction in the central nervous system. By proper technic, however, acute thrombi and chronic fibrous changes in the lumen of the vessel, stasis, dilatation and engorgement proximal to the thrombus, extravasation of blood and accumulation of pigment may all be recognized more clearly than in most organs.

All these processes have been described before in cases of multiple sclerosis, though not always clearly. The hypotheses that they are all secondary to local inflammatory changes and that they contribute to the formation of plaques merely by permitting the escape of toxic material both seem unnecessary, in view of the production of plaques in animals by experimental venous obstruction and the observation that the acute stage of such a process occurs in the human brain as the result of venous thrombosis.

There is no indication that the primary cause of the thrombosis exists in the wall of the vessel. It appears that it should exist therefore in the circulating blood. Attempts to demonstrate an adequate cause for the occurrence of spontaneous thromboses by chemical and biologic methods are in progress in this laboratory.

A question inevitably arises from consideration of the data presented here: Are not the vascular changes described—thrombosis of small veins, dilatation and obliteration—reasonably common postmortem observations in various organs, including occasionally the brain, and are they not to be ascribed to the terminal infection or marasmus? Unquestionably, they do occur and are related to the illness through which the patient has just passed, and this fact may be taken as supporting the theory of formation of sclerotic plaques which has been outlined here. If thrombi sometimes form in the cerebral venules during any one of a variety of fatal illnesses, they doubtless occur during the course of infection or other conditions which are not fatal. Conceivably, some of these thrombi are too small to cause parenchymal damage, but if they exceed a certain size, they must inevitably cause lesions. Evidence has been presented [1b] that such lesions will display all the characteristics of sclerotic plaques. Dr. Leo Alexander and I have examined as a routine, with the methods used to demonstrate thrombi in this study, practically all blocks of brain tissue cut in the course of an active neuro-

pathologic service and have failed to observe any that met the criteria established which were not accompanied by lesions of one or another of the types that have been described.[37]

Question of Vascular Spasm.—It has been suggested (e. g., by Jelliffe,[44] Wetherell[45] and Petersen and Milliken[46]) that spasm of the vessels of the white matter might lead to sclerotic plaques. Such a possibility appears to me unlikely. In the first place, although the cerebral vessels undoubtedly possess the power of contraction, it is small compared to that of vessels elsewhere in the body[47] and probably less in the white matter than in the cortex.[48] In the second place, it appears probable, for reasons already given, that the obstruction to circulation in multiple sclerosis is on the venous side and that the cerebral veins contain little or no muscular tissue. On the other hand, it is probable that anything which decreases the rate of cerebral circulation favors the occurrence of thrombosis.

SUMMARY

1. The existence of vascular obstruction, dilatation and proliferation, and of perivascular hemorrhages and deposits of blood pigment in the lesions of "encephalomyelitis" and multiple sclerosis has been affirmed by many writers.

2. By the use of refined technic, the existence of thrombi in various stages may be demonstrated in cases of "encephalomyelitis" and multiple sclerosis. The frequent occurrence of vascular engorgement and perivascular hemorrhages in acute lesions and of vascular obliteration in chronic lesions is confirmed.

3. Previous studies, experimental and pathologic, have indicated that vascular changes such as those observed are adequate to cause the alterations in the parenchyma characteristic of the two diseases.

4. Thrombi also are occasionally to be found in organs other than the nervous system in cases of multiple sclerosis.

5. The primary abnormality is to be sought probably in the clotting mechanism of the blood.

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44. Jelliffe, S.: Emotional and Psychological Factors in Multiple Sclerosis, A. Research Nerv. & Ment. Dis., Proc. **2**:82, 1921.

45. Wetherell, F. S.: Multiple Sclerosis: Cervicodorsal Sympathectomy as a Relief Measure; Report of Case, J. A. M. A. **102**:1754 (May 26) 1934.

46. Petersen, W., and Milliken, M.: The Patient and the Weather: Mental and Nervous Diseases, Ann. Arbor, Mich., Edward Brothers, Inc., 1935, vol. 3.

47. Pool, J. L.; Nason, G., and Forbes, H.: Cerebral Circulation: XXXIII. The Effect of Nerve Stimulation and Various Drugs on the Vessels of the Dura Mater, Arch. Neurol. & Psychiat. **32**:1202 (Dec.) 1934.

48. Finesinger, J., and Putnam, T. J.: Cerebral Circulation: XXIII. Induced Variations in Volume Flow Through the Brain Perfused at Constant Pressure, Arch. Neurol. & Psychiat. **30**:775 (Oct.) 1933.

NOTE.—Since this article was submitted for publication several papers bearing on the same subject have appeared or are in press.[49]

DISCUSSION

DR. L. ALEXANDER: Dr. Putnam has referred to some work in which I took part. When Dr. Putnam last year opened a neuropathologic laboratory within the gates of the Mallory Institute of Pathology at the Boston City Hospital it gave opportunity to study more cerebrums from patients who had suffered from various systemic diseases and died in the wards of the medical and surgical departments of the hospital. My associates and I collected about 6,000 slides in 182 cases. Dr. Putnam's work suggested particular attention to vascular occlusion, associated especially with arteriosclerosis but also with other diseases leading to thrombosis of cerebral vessels.

The slide demonstrating petechial hemorrhages, closely resembling those in postvaccinal encephalitis, was from the brain of a woman aged 78, who had extensive thrombosis of the superficial veins of one hemisphere. Two other cases in which plaquelike lesions were observed in the white matter were instances of pneumococcic and streptococcic meningitis, with thrombosis of the superficial veins. The complete picture of demyelinization in these plaques resembled that in plaques of multiple sclerosis. In cases of meningitis in which there is no complication such a picture is not observed. A few days ago a picture of diffuse sclerosis was seen in the brain of a man of advanced age, with multiple thrombosis of the meningeal arteries. These cases confirm fully Dr. Putnam's conclusions regarding the mechanism of plaquelike and diffuse demyelinization of the white matter of the brain.

DR. K. FINLEY: My colleagues and I were unable to explain the subependymal glial reaction. Dr. Adler's sections, however, show that this subependymal reaction was related to the veins which lie immediately beneath the ependyma. This would correspond somewhat to the subpial glial reaction which we observed only about veins of the cord as they passed into the pia-arachnoid.

DR. H. H. MERRITT: Dr. Putnam was one of the first to draw attention to the venous side of the cerebral circulation. His work has shown what other neuropathologists have missed because they have not studied sections appropriately stained to bring out the vascular lesion.

DR. T. J. PUTNAM: A point which I neglected to mention in the paper and which is often brought up in informal discussions of the subject is that almost any pathologist on seeing these thrombi is likely to remark that they are not different from thrombi which may often be seen diffusely distributed through many organs of patients who die of infectious disease. I agree with this, but I believe that they occur not only in patients who die but in those who survive and not only in infectious disease but under other conditions. I believe further that when they occur in the central nervous system they leave small or large and few or many lesions of the general type which have been shown tonight.

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49. Merritt, H. H.; Putnam, T. J., and Campbell, A. C. P.: Pathogenesis of the Cortical Atrophy Observed in Dementia Paralytica, Arch. Neurol. & Psychiat. **37**:75, 1937. Alexander, L., and Myerson, A.: The Mineral Content of Various Cerebral Lesions as Demonstrated by the Micro-Incineration Method, Am. J. Path., to be published. Putnam, T. J., and Adler, A.: Vascular Architecture of the Lesions of Multiple Sclerosis, Arch. Neurol. & Psychiat., to be published. Putnam, T. J.: Lesions of "Encephalomyelitis" and Multiple Sclerosis: Venous Thrombosis as the Primary Alteration, J. A. M. A. **108**:1477 (May 1) 1937.

HEALTH AS A PSYCHIC EXPERIENCE

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One generally takes it for granted that the person who has no disease should feel healthy and that the person with an organic lesion or dysfunction should feel sick. One is inclined to consider the experience of one's health as an immediate reflection of the physiologic or the pathophysiologic state of the body. A person who has lost one leg and walks with a prosthesis or with crutches is not sick. Whenever there is a stabilized defect, either in form or in function, the organism adapts itself psychologically, as well as physiologically. The feeling of health seems to be the expression of a newly won stabilization in the psychophysiologic organism.

Lower organisms, in which the possibilities of regeneration are almost unlimited, react to a considerable loss in the material of the body by melting the remaining material into the diminutive picture of the intact organism, even without food. When the egg of an echinoderm is divided in half, a complete embryo develops. Lizards regenerate their tails. When one leg of a dog is amputated, the adaptations are adaptations in function and attitude. They occur when the contact with the ground is lost. The loss of each leg necessitates a different adaptation. Walking, trotting and galloping are possible with three legs.[1]

The new equilibrium of the organismus is therefore reached either by growth and regeneration or by a change in function and attitude. The experience of health is the expression of such adaptive tendencies in the psychologic sphere. The psyche tries to maintain it, even when there exists a severe organic disease. Psychiatrists and neurologists have always been interested in the fact that disease and suffering occur in relation to individual problems, and organic disease has even been considered as an expression of the tendency to fall ill. It has, however,

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1. Bethe, A., and Fisher, E.: Die Anpassungsfähigkeit des Nervensystems, in Bethe, A.; von Bergman, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1930, vol. 15, pt. 2, pp. 1046-1130.

been overlooked that there exists not only psychogenic disease but psychogenic health. The problem of physical health has never been studied in its psychologic aspect.

Even in the completely healthy person, continuous sensations from various parts of the body offer themselves. One is fatigued and has a little pain here and there—a slight headache, some disagreeable abdominal feelings and itching. In order to experience health, one has either to coordinate the smaller sensations into a unit or to make the attempt to remove them completely from the field of consciousness and forget about them. The vegetative system offers a great number of sensations which might impair the feeling of well-being: hunger, thirst, the urge to urinate and defecate and, finally, the smaller stimuli arising continually in the genitals. The experience of health can therefore be maintained only in a continuous dynamic interplay. When this dynamic interplay is disturbed by inner conflict, the smaller stimuli obtain another dynamic significance. Although this is unquestionably not the only source of the so-called conversion symptoms, it is a contributing factor.

If serious disease threatens, the person still tries to maintain the experience of health by minimizing the organic discomfort or by neglecting it completely. In cases of far progressed cancer this tendency is shown clearly.

A workman aged 60, with carcinoma of the stomach, said: "I was operated on about eight months ago for a tumor. I had pain before. Everything I ate went through me. Now nothing will go through me. My bowels are not allright. I had pain. I vomited always. I did not think it was dangerous. It got worse. I don't know why. I came into the hospital to be cured. They gave me a spinal anesthesia. I was not afraid at all. I had confidence. When they give me a physic now, it tears me to pieces. Otherwise, I have no pain. I thought I had an ulcer, but I know now it is a tumor. It feels like a growth. When I get well, I will go to work again. I am pretty weak now, although I eat fairly good." When asked what he enjoyed most in his life, he said: "Going out with a lady friend on Saturday nights." If three wishes could be fulfilled to him, he would wish to be strong, to go to work and to have a few more good years. "I have suffered enough." He said he felt better, "although I had a bad day today." The patient had a sister whom he liked very much. He was not married. During the last few years, he had had no "lady friends." He had a hopeful attitude, although a slight apprehension broke through occasionally.

The attitude of this patient is fairly typical of that of persons with severe organic ailments. One would expect that the patient would know that he had a malignant growth. But he did not acknowledge the physical disease fully. He minimized his symptoms and deceived himself about his physical weakness. He wanted to maintain the experience of health against heavy odds and was partially successful. The

psychic organism maintains its integrity better than the physical organism. So far as the patient did not allow himself to know how sick he was and how badly he felt, one has the right to speak of repression. The repression uses narcissistic libido as one of its motors.

This connotation does not explain the facts fully. The organic disease and the symptoms produced by it are, in their very nature, not a personal concern of the subject, who is moved deeply only by the moral problem. Organic disease lies not in the center of the personal life but in the periphery.[2]

I have spoken of the circle of the ego (*Ichkreis*). From immediate experience, one knows whether one is touched in the core of one's personality, whether or not the experiences are near the nucleus of the ego. In this respect, one's problems, emotions, feelings and attitudes belong closer to the nucleus of the ego than do the experiences relating to the outward world and to one's own body. Not all sensations have the same distance from the imaginary center of the ego. Pain, sexual excitement and anxiety are in the center of the personality. The self is completely in them.

Some parts of the body are nearer the center of the ego than others. It makes a great difference which part of the body has been mutilated, and the statistics of postoperative psychoses show that mutilating operations provoke psychosis in a higher percentage of instances than nonmutilating procedures. Operations on the genitals, breasts and eyes threaten parts of the body which are nearer the center of the ego than others. In schizophrenia and neurosis the complexes lie in the center of the personality. The experiences associated with organic lesions of the brain, such as dementia paralytica, arteriosclerosis and injury to the head, concern material which is rather impersonal. It has nothing to do with the vital problems of the personality. In organic lesions of the brain the psychologic experiences are in the periphery. Patients with organic disease are generally much more objective toward the disease than those with psychogenic illnesses. It is as though the organic disease would not be so much one's personal affair.

A patient aged 35 with nephritis, which is improving, said that he never felt really sick but merely had difficulties in breathing. He felt that he would recover. He did not worry even when he became blind (retinal hemorrhages). He knew that he would go to the Bellevue Hospital and that it would be the concern of physicians to cure him.

2. Schilder, P.: Der Ichkreis, Ztschr. f. d. ges. Neurol. u. Psychiat. **92**: 644-654, 1924. The term ego is used here not in the psychoanalytic but in the general psychologic sense. If one tried to correlate the connotations, one would probably consider the psychoanalytic ego nearer to the periphery of the circle of the ego than the id.

The difference in attitude is particularly clear in cases of impotence. The patient with organic impotence has an almost heavenly patience in relation to this occurrence. The organic disease is in the periphery of the personality. The psychogenic disorder occupies its center. When one studies the history of the conversion symptoms, one sees that at first the patient is much concerned about his problems. He is worried as a person. After he has succeeded in forming the conversion symptom, he cares less for it than one would expect. Patients with hysterical hemiplegias are almost as happy as those with an organic lesion. The problem has wandered from the center to the periphery. In accidents, such as injuries of the head, an organic disease starts in the outward world and in the body and not with the problems of the personality. The subject merely becomes secondarily impressed by the disease. I believe that many organic diseases belong in this category and that in almost all of them such an extraneous factor participates. In these cases the experiences wander from the periphery to the center. Psychic life is a continuous movement of the experiences from the center to the periphery and back. The body and the organic disease belong in some way more to the periphery than to the center of the personality.

Not only in association with carcinoma and nephritis are such attitudes to be found. One meets the same attitude in cases of organic heart disease (unless pain and anxiety come into the foreground).

A man aged 64, of Jewish extraction, had coronary occlusion, which was followed by a period of disturbances in memory, with confusion and confabulation. At the time of examination he was clear, oriented, talkative, jocular and euphoric and even showed some memories of the time when he was confused. He reported that his disease started with difficulty in breathing. "I could not get air. I certainly thought I should die. Who would not be afraid?" The patient talked without sign of real emotion and was rather objective. "I felt only a heart burn. I had no pain. I felt so bad, I wanted to die. What can I do any more after I am 64? I can't work; I can't make money. I have nothing to live for. I want only that my wife does not go to charity. My wife should have support. I can't sleep; I struggle to get well." The patient was at a loss, when he was asked in what way he struggled to get well. He said merely that one has to go early to the hospital.

Many other patients show this attitude, in a still more outspoken way. It is not necessary to increase the material, since Fahrenkamp [3] has demonstrated, in an extensive study, that patients with organic heart disease show, in striking contrast to the objective findings, little or no consciousness of disease and, consequently, no insight. Complaints (shortness of breath on exertion) are minimized or dissimulated. On the contrary, in neurotic cardiac conditions, one usually finds a marked

3. Fahrenkamp, Karl: Der Herzkranke, Stuttgart, Hippokrates-Verlag, 1931, pp. 1-287.

subjective experience of illness (*Krankheitserlebnis*) referred to the heart or to the circulatory system.[4]

A particularly striking instance appears in the attitude of patients with cerebrospinal meningitis. It is rather typical that when they recover they remember hardly anything but headaches. They never have had any feelings which they attributed to severe organic disease.

A girl aged 19, who had been feeling ill for three days before admission to the hospital and who complained of headache and vomiting, did not talk at the time of her admission. The somatic picture and the spinal fluid findings were typical of those in meningococcic meningitis. The stupor and drowsiness subsided. Twelve days after admission, she answered the question: "How did you feel?" with "Pretty good; I don't know what happened to me." In subsequent days she remained clear and felt well; she minimized the headaches and did not have any conception that she was seriously ill.

A woman aged 40, who was alcoholic, entered the hospital after wandering around for three days, in a slightly delirious condition with the complaint that she had a pain in her back and that her eyes were sore. She had typical meningococcic meningitis. With the disappearance of the sign of meningitis, after fourteen days, the patient's condition became progressively clearer, and she had no particular appreciation of her illness. She knew that she was confused but did not remember her physical discomfort, except the pain in the back.

A man aged 43 was found sitting on a doorstep, in a stuporous state. His employer had found him "groggy." In the hospital he was clouded, stuporous and lethargic. The condition was typical cerebrospinal meningitis. He improved after a week. His final attitude toward his disease is reflected in the following remarks: "I don't know how I got here; the last thing I remember is when I left for work. They told me to go home because I wasn't able to work. I was just dizzy, dizzy all over. Sure, I had a headache." He has amnesia for the stuporous period.

One might object to these illustrations and emphasize that organic toxic changes are seen in the brain in meningitis. This fact is not denied. The attitudes are not created merely by the toxic factors. It is a general, but often neglected, principle of psychopathology that organic and toxic changes do not create the problems and attitudes of the patient but bring them more into the foreground of consciousness. The organic change is merely a sensitizer. It is true that the various organic influences sensitize the brain in different directions, and it is probable that the wish to be healthy is helped by the majority of toxic influences of various kinds, which is in itself an important problem. The euphoria and optimism of the patient with tuberculosis, which have for a long time been in the center of medical attention, are therefore merely a specific expression of the general problem of the psychologic attitude in organic disease. With the progress of organic disease and

4. Dunbar, H. Flanders: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1933, New York, Columbia University Press, 1935, pp. 1-595.

the more severe impairment of function, the increasing feeling of weakness, the mechanism of neglect—minimizing and repressing of the organic disease—becomes insufficient. A more elaborate defense is necessary to retain the experience of one's health.

A woman aged 70, with extensive carcinomatous metastases, was mildly disoriented but was sufficiently composed that she could be kept in the medical ward. Although very weak and unable to get up, she was happy and did not realize her weakness and disability. She was deeply attached to her son, who visited her about twice a week. "I am happy, very happy about my son. He gives me food; he visits me. I have no pain; I am not sick; I can eat." When asked about relatives, she said, in a deprecatory manner: "My poor sister was very sick. She is in heaven; I have no parents; they are dead."

Thus, the patient readily acknowledged the disease and death of others but escaped herself into an infantile state of oral satisfaction. This may be stated as a variation of Descartes' statement, *"Cogito, ergo sum,"* thus: "I eat, and therefore I exist and am healthy." Deutsch [5] reported the case of a patient dying of heart disease who regressed to the oral level of libido and revived in her fantasy an old love relation to a brother. Another patient, with severe carcinomatous metastases, revived before death an infantile love relation with a sister.

Patients with severe illness escape suffering from organic disease by regression. The regression revives infantile love relations and passes finally to the oral stage.

In another group of cases the mechanism of projection plays the outstanding part. Projection also, of course, is based on regression. However, one deals here with such an important primitive mechanism that an independent discussion is necessary.

In an earlier study [6] I observed a patient with far progressed tuberculosis who heard the voice of God that he should take a fresh air cure, in order to recover. He was born again, in order to rid the world of tuberculosis. He said that his brother, to whom he gave his name, was sick, but not he himself. He called himself spirit, savior and Jesus Christ, who saved humanity with himself. The mechanism of projection is obvious here.

A patient aged 50, with carcinoma, felt she was attacked and defended herself by violent aggression.

Another patient aged 58, with cancer of the stomach, said that some one wanted to murder her but that she had recovered from death and from tapeworm. Immediately before her death, she considered herself recovered and said she had saved the whole world. The regression was connected in this case with not only projection but narcissistic ideas of grandeur.

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5. Deutsch, Felix: Ueber Euthanasie, Internat. Ztschr. f. Psychoanal. **21**: 220-234, 1935.

6. Schilder, Paul: Ueber Stellungnahmen Todkranker, Med. Klin. **23**:783-786, 1927.

Regression to narcissism and projection is in no way limited to the most severe conditions. T. Wortis has shown at the Bellevue Hospital that in psychoses associated with heart disease the mechanism of projection plays an outstanding part. The patients feel persecuted, followed and threatened and sometimes they even attempt to get rid of the anxiety by projecting it outside. It is easier to defend oneself against persecution than against disease. Patients maintain the feeling of health by the mechanism of projection.

For instance, a patient of Wortis said: "That man Jack over there, a porter or something, had the most brutal manner and tried to intimidate me; it looked like an armed projection—there were people there with guns."

Another patient said: "For several nights I have been followed; they are trying to put something over on me."

Projection helps even against pain. It is known that when persons fall asleep, physical pain is projected into others. I have previously observed patients with gynecological disease who referred the pain to beatings by little men. Cases of pernicious anemia are of special interest from this point of view. Bender [7] has pointed out that patients with pernicious anemia often refer their disturbances, especially the nervous complications, to hostile influences coming from the outside world. Pictures may occur which show a great similarity to paranoia. A short time ago, I observed a patient with pernicious anemia who in the beginning of the illness complained to the police that there was always a smell around from brewing hootch.[8]

Helen M., aged 54, was admitted to the hospital on March 29, 1934, with the statement that she was suffering from hallucinations of smell and had the delusion that numerous airplanes distributed foul odors. She was irritable and depressed and complained bitterly about her mother, who had stated that she had made suicidal attempts. The patient said: "It was a big stroke on her part; she was very vicious to me. It was her aim to put me out. She is a combination of a tigress and a leopard—very obstreporous and very spatty. She wrecked my life. There is an irritating smell which burns my throat and swells my intestines. The airplanes give out a vapor as they pass me. They swell me up and pull all my

7. Bender, Lauretta: Psychoses Associated with Somatic Diseases That Distort the Body Structure, Arch. Neurol. & Psychiat. **32**:1000-1029 (Nov.) 1934.

8. The extensive literature on psychosis associated with pernicious anemia has lately been reviewed by Karl M. Bowman (Am. J. Psychiat. **92**:371-396, 1935). Projection is not the only mechanism by which patients with pernicious anemia defend themselves. In the beginning of the disease the feeling of weakness is often overcompensated. In fantasies of wish fulfilment one patient in the clinic elaborated a story that she was a daughter of the czar and neglected completely her severe paraplegia. Astasia-abasia, not rarely observed in the beginning, not only serves the tendency to make it clear to others that the patient is sick but probably gives the patient a feeling of consolation, since he feels that he has provoked these symptoms.

bones out. I am very susceptible. These smells swell me up and stop my heart, turn my ankles and pull them out of place. They are very big from poison gas. When the poison gas goes out, I can move my feet. I want treatment immediately. I had all my teeth extracted. My mother would steal my food. She is a racketeer. She has always been that way, but I found it out two years ago." The patient was irritable and talkative but not confused. She was also extremely irritable toward the physicians and nurses. The report of the mother was: "There are no nervous and mental diseases in the family. She lived with me; she was very bright; she was a good scholar and always wanted to learn; she was going to be a teacher. Then she got sick. Her nerves gave out, and she was told to stop. Between 17 and 20, she worked as a bookkeeper. Up to the time of the operation, she had been working actively. The operation was an intestinal operation. The following year, 1917, her ovaries were taken out. She has been sick for fifteen years. She has been devoting all her time to irrigating her nose and throat. She used 150 pounds of soda in one month. She used mild silver protein for five or six years. Her nose was operated on in 1914. She would leave her meals five or six times to irrigate. During the last six months she has been more cranky than ever. She says every one in the house is a spy and is trying to murder her. She complained that the people around put disinfectants in her room. She cussed and called me a thief."

Physically, the patient showed a high degree of emaciation, cyanosis, pallor and argyrosis. There was edema of the legs and thighs. The tongue was smooth and glazed, but not inflamed. There were sinus tachycardia and slight enlargement of the heart. A blood count revealed 2,360,000 red cells and 30 per cent hemoglobin. The leukocytes numbered 7,000, with 82 polymorphonuclears, 16 lymphocytes and 2 transitionals. A blood smear showed marked poikilocytosis and numerous cylindric cells. The picture was one of idiopathic hypochromic anemia. From one to three of the fingernails on each hand showed marked thickening and curvature.

The glossitis and type of anemia were compatible with a diagnosis of idiopathic hypochromic anemia—the Plummer-Vinson syndrome. The congestive heart failure can be accounted for by the severe anemia, as well as by protein deficiency. The argyrosis was probably associated pigmentation rather than poisoning with a heavy metal.

After stormy periods of paranoid excitement, with shouting, accusations, etc., the patient's mental status improved markedly. She became more agreeable and lost her delusions. Mental improvement paralleled physical recovery, under treatment with blood transfusions, iron, liver and special diet. The case is of special interest, since the patient considered the oral symptoms connected with the anemia to be an expression of hostile influences from gases.

This case of Plummer-Vinson's anemia [9] is remarkable for the clearness of the projection mechanism. I come, therefore, to the conclusion that the experience of health can be maintained by the mechanism of projection. If the projection is incomplete, the discomfort of disease is experienced as the result of hostile influences. If the projection works more completely, the patient feels that not he but others are sick. In the beginning, his opinion on this point may be uncertain. Finally,

9. Hurst, Arthur A.: Some Disorders of the Esophagus, J. A. M. A. **102:** 582-587 (Feb. 24) 1934.

not only his own disease but the diseases of others are cured. With more complete projection, narcissistic ideas of grandeur come more and more into the foreground. One might ask why these elaborate mechanisms should be necessary in order to maintain a feeling of health, if organic disease is in the periphery of the ego. The experiences in the periphery of the ego, the sensations coming from the body, are in themselves not always at the same distance from the nucleus of the ego. Pain itself has the tendency to progress from the periphery into the center and to fill the whole personality. Any physical change transgressing a certain quantity will provoke an overflow from the periphery to the center, and the psychic mechanisms discussed have as their aim the defense of the center of the ego against inroad from the periphery.

Two symptoms provoked by organic changes make defense necessary. One, as mentioned, is pain of major degree, and the other, anxiety. If the pain is not severe, as in pneumonia, the patient may at the height of the discomfort pass into a delirious episode. It is interesting that patients in delirium forget about pain, and it is also characteristic that in the report they always emphasize that they knew about the disease and pain the moment the delirium set in. I give here an excerpt from a protocol.

A woman aged 60, who had just recovered from lobar pneumonia, talked continually. She said: "Last year I hardly escaped pneumonia. This time I was hot but had no pain." (Fever?) "I had a cold." (Would you not be afraid of pneumonia?) "I could not stand pneumonia." She said she saw another woman strapped down, with pneumonia. A few minutes later, however, in the course of conversation, she said: "They told me I had pneumonia, type 3."

Since it is known that the delirious patient with pneumonia often wanders out of bed and endangers his life, it is obvious that the psychologic defense might be detrimental. One comes to similar conclusions regarding anxiety. It has already been mentioned that the patient with heart disease defends himself against anxiety by projection. If the anxiety surpasses a specific degree, the defense becomes insufficient. It is probable that an acute onset of the anxiety contributes to make the psychologic defense impossible. This is true in angina pectoris, in which the feeling of anxiety is all pervading. I am not so much concerned here with whether anxiety is, as Braun [10] stated, a sensation coming from the heart or whether, as Hausner and Hoff [11] said, is due to edema of the brain stem and the medulla oblongata. I have no doubt

10. Braun, Ludwig: Herz und Angst: Eine ärztlich-psychologische Studie, Vienna, Franz Deuticke, 1932.

11. Hausner, Erich, and Hoff, Hans: Zur Pathogenese des Angstgefühls im Angina-Pectoris-Anfall, Ztschr. f. klin. Med. **125**:493-507, 1933.

that central factors participate in this feeling of anxiety, which is connected with the conviction that one must die. Anxiety and the feeling of impending death and destruction have been noted not only by Hausner and Hoff in association with tumor of the posterior fossa, but by me in cases of chronic encephalitis with vasovegetative phenomena. It is characteristic that the patient feels utterly helpless when the anxiety comes over him and is ready to give up completely. One may draw the preliminary conclusion that the physician faces the duty of helping the patient when the psychic defense is so utterly abolished.

At any rate, intensive pain and anxiety are organic symptoms against which psychic defense is insufficient. One might doubt the validity of the formulation that the patient is trying to neglect organic disease and defend himself against the knowledge of being organically ill and might point to the fact that so-called psychogenic symptoms are common in organic disease. It is doubtful whether the term psychogenic symptom is always used correctly. Human beings must have attitudes, and these attitudes are psychic. A symptom is always a psychic attitude and not merely a reflection of prospective observations at the autopsy table. People cannot help having problems, and these problems are part of their attitudes. It is true that there are patients with organic disease who not only have an exaggerated appreciation of the disease but demand the attention and pity of others. Patients with pernicious anemia may present conversion symptoms, but these symptoms almost invariably occur at a time when the organic disease is not yet fully developed. In the clinic at Vienna my associates and I always suspected beginning multiple sclerosis when motor conversion symptoms were particularly outspoken. The complaint of the patient with organic disease is often in reverse proportion to the degree and severity of the disease. Psychogenic symptoms may occur also during convalescence.

A patient with tuberculosis was filled with fear of death and complained of dizziness, weakness and inability to concentrate. The tuberculosis has been cured. Prior to the time of the illness, he had been much interested in sports, and he was narcissistic about his body. He was much moved by the fact that his sister had died of tuberculosis.

In another case, a severe neurosis, consisting of the fear of infection with bacteria, followed herniotomy, which was not completely successful. The patient was an athlete, with extreme narcissism, whose life was shattered when it was made clear to him that he could not excel as a baseball player.

A patient aged 36, who had recovered from acute nephritis in which the systolic blood pressure rose to 180, complained that his chest and arms had flattened and that he felt that his breathing apparatus did not belong to him. He also said that his penis looked smaller and thinner than normal. He was at the time rather unexpectedly at a peak in his career. His complaints came after the organic disease had passed.

The appreciation of organic disease varies according to the general state of mind.

Rose C., aged 50, had acquired rheumatic heart disease in early childhood. She had occasional attacks during which she could not breathe and felt that she would die. She felt then that her heart enlarged, as though it smothered the windpipe. For the most part, however, she did not feel much beside weakness. After the death of her mother, in 1926, she had a "nervous breakdown." At that time she first became conscious of the heart disease. For the last two years she had had no attacks, but in connection with trouble with a sinus, which made irrigation of her nose necessary, she acquired the idea that she had a "terrible disease" and talked of it to every one. She thought that her finger was rotting away. (A religious ring on her finger turned black.) At this time she felt at first that her heart was bad. The more depressed she became the less she thought about her heart. Finally, it was as though her heart had turned to stone and would not give any sensations. At the time of examination the patient was happy and content. She had no sensations concerning the heart. On later observation, the complaints concerning the heart varied according to her moods.

A patient with severe decompensation complained that she had palpitation on Wednesdays. Wednesday was visiting day, and she expected the visit of her husband. Once she was disappointed.

A man aged 45 had never had complaints of any kind. One night he had to leave his apartment, which was on fire, and on subsequent nights he dreamed with anxiety about the fire. He experienced difficulties in breathing. The condition was severe hypertension.

It would be easy to cite many more instances. It is clear that the experience of health and disease is dependent not merely on the so-called organic findings but on the problem of the person. There is a tendency for the patient to maintain the experience of health, even in the face of severe organic disease, and for severe organic disease not to be the basis for conversion symptoms. Organic ailments of minor degree may be the nucleus of conversion symptoms or may be used according to the general attitude of the subject. Organic symptomatology of severe degree is never, and cannot be, without relation to the problems of the personality.

I speak of the experience of health, but one might well say that there are many components in this feeling of health. There is the general feeling of vigor. Kinnier Wilson and Cottrell [12] spoke of eutonia. There are the sense of happiness (euthymia or euphonia) and the conviction that whatever may be realized as discomfort will not be lasting. They also spoke of optimism and *spes sclerotica*. I wish to emphasize

12. Wilson, A. Kinnier, and Cottrell, Samuel Smith: The Affective Symptomatology of Disseminated Sclerosis: A Study of One Hundred Cases, J. Neurol. & Psychopath. **7**:1-36, 1926. The authors have described well the psychic attitude of the patient with multiple sclerosis, but they were not interested in the problem from a general point of view and have therefore not emphasized that the attitudes in multiple sclerosis are merely a specific manifestation of a general problem.

that these three experiences go together. They are a unit, although one or the other may be outstanding. Wilson has pointed to the importance of the psychiatric findings in multiple sclerosis. He found that in the phase of serious organic disability patients retain the experience of health; he attempted to find an organic explanation for this fact. He expressed the belief that a lesion of the thalamus has such an influence. I have emphasized that this attitude is a general experience of the patient who is organically ill. It is true, however, that the patient with multiple sclerosis shows this phenomenon in a particularly strong degree.

I come to the conclusion that a lesion of certain parts of the brain may aid psychic attitudes which neglect the organic disease. For reasons I cannot discuss here, I am inclined to believe that it is the lesion not of the thalamus opticus but of the periventricular gray matter which has such an influence. Since no definite proof is possible at present, one must be content with the general statement that noncortical lesions may aid in the experience of health.

One is on safer ground in discussing the psychic attitude in cases of sensory aphasia. It is typical of sensory aphasia that the patient shows a multitude of drives and impulses, not only in the sphere of language but in the total field of motility. His euphoria is outspoken. He often overlooks his defect completely, especially in the beginning. In the later development of the disorder, he may experience difficulties in finding words, but he will not be disturbed by it. He will remain decidedly optimistic and will retain the feeling of health. I reproduce a protocol in a case of injury to the head.

A man aged 40, who had no remembrance concerning the accident and no insight into the fact that he was sick, had difficulties in understanding and in finding words. Several days after the accident the pain asymbolia, which had been present in the beginning, disappeared. When the patient was asked, "Are you happy?" he said: "Well, no; I could be happier. There is something I would like to know, how to be happier. (In what way are you not happy?) For one reason, because lying here and not making steps forward, I am not happy. (Are you sick?) I am not really sick. I am recovering from a road that means more significance. (Are you sick?) Not really sick; not now. I am healthy. I feel strong, and I wish you that same identical thing. That's all in happiness is to seek and find happiness in life, but trouble is to get established, so as not to seek. It does not make any difference what people you come in contact with. White or colored. I will never ignore any colored race but interview them. It is all cycles of business, commercialized. Undoubtedly, I may be wrong in this." When he was shown a key, he made a sucking motion and said: "Maybe it is a good-luck stone I am kissing. I have a ring with a flowery design like that. There is no asking towards. Let's talk about something else. (Again shown a key.) It might be luck, I suppose. (Again shown a key.) It looks like a key. (Shown a handkerchief.) Handparchef or handkerchief. (Shown a pen.) A tool piece of your own. I am just jumping at the analysis."

It is remarkable that patients of this type keep their euphoria and their optimistic attitude, in spite of the headache they experience at the time. It is also characteristic that the patient named a key a good-luck stone.

It would be easy to increase the number of instances. One may find others in a previous paper.[13] I emphasize, of course, that these psychic attitudes are in no way restricted to cases of sensory aphasia which occurs after injuries to the head. Every lesion of the Wernicke region provokes the same picture, with the same characteristic psychic attitude. The attitude therefore is due to the local lesion of the brain.

The importance of these findings becomes clearer if one compares the attitude of the patient with sensory aphasia with that of a person with so-called motor aphasia, who is moody and depressed and has a feeling of being sick, with normal or exaggerated consciousness of his deficiency.[14]

Paraphasias and syntactic errors may disappear, and the general attitude of euphoria, the feeling of health, may remain. There is an undoubted relation between the Wernicke region and the experience of health. I have observed cases of injury to the head in which pictures of this type occurred, without definite signs of aphasia.

A man aged 42 with a longitudinal fracture of the skull extending through the squamous portion of the right temporal bone, about 2 inches (5.08 cm.) long, and with xanthochromic spinal fluid, talked continually and was flighty and euphoric. He gave details about his past. He did not show definite signs of aphasia, although grammatical construction was sometimes incomplete. He copied correctly but added occasional words. When asked what an envelop was, he said: "We don't use them in Ireland much, an envelop—it is old—some of them are in the mountains." When asked what a president was, he said: "It is a peasant—a president is a man that rules your country. A president—that is all he is." When asked to name the year, he said: "That year is good enough." He showed pain asymbolia. The patient was examined twenty days after the injury occurred.

It is interesting in this connection that, according to my previous formulations, there exists a center in the supramarginal gyrus a lesion of which impairs appreciation of pain. Other parts of the parietal lobe have to do with the appreciation of defects, and a local lesion may prevent such appreciation. It is to the merit of my teacher Gabriel

13. Schilder, Paul: Psychic Disturbances After Head Injuries, Am. J. Psychiat. **91**:155-188, 1934.

14. I am studying at present a group of patients in whom motor aphasic signs, increased sensitivity to pain, exaggerated mimic expression and gestures are in the foreground. Although these patients have full insight into the defect, they are euphoric and have the general comportment of well-being. Reference may be made to a previous paper (Cortical bedingte Steigerung von Schmerzreaktionen, Ztschr. f. d. ges. Neurol. u. Psychiat. **132**:367-370, 1931).

Anton to have pointed to the general importance of this fact.[15] Since I have discussed this problem at length on previous occasions,[16] I shall indicate here only generally the importance of the parietal lobe for the construction of the body image and for appreciation of one's own health and disease. Many phenomena in association with organic disease of the brain in which the lesion is more or less diffuse can be explained in this way.

One can understand better, for example, how it is that patients suffering from injury to the head without sensory aphasia are so often not concerned about the injury. Even the retrograde amnesia in cases of injury to the head can be understood better on the basis of the general theory of the experience of health. I come, therefore, to the conclusion that the experience of health and disease, although an attitude of the personality, is dependent on the function of specific centers in the brain, among which the Wernicke region is the most important.

It would be easy to extend the discussion into the field of psychiatry, but these remarks are devoted chiefly to the problem of organic disease which is not dominated by psychosis. Suffice it that in organic diseases of the brain the experiences and disturbances are, as is expected, in the periphery of the personality in the sense in which it was defined, whereas a psychosis with which no gross anatomic lesion is associated is in close relation with the center of the personality.

Are these merely theoretical discussions, or can one deduce practical conclusions? I think that knowledge of the attitudes in organic and psychogenic diseases is of great diagnostic importance. One must understand also the specific attitudes connected with specific organic diseases. One will then understand better psychogenic pictures and the specific relations to beginning organic disease. There is still lacking a symptomatology of internal diseases from a psychologic point of view.

I believe that such a symptomatology of internal diseases, evaluating the psychologic structure of the pathologic experiences of the person with organic illness, will be of indispensable value not only for diagnosis but for the treatment of the patient. It is trite to say that every sick person needs psychologic help. One can be more specific, since there is a tendency of the patient with organic disease to forget the disease, or

15. Anton, Gabriel: Ueber Herderkrankungen des Gehirns, welche vom Patienten selbst nicht wahrgenommen werden, Wien. klin. Wchnschr. **11**:227-229, 1898; Ueber die Selbstwahrnehmung der Herderkrankungen des Gehirns durch den Kranken bei Rindenblindheit und Rindentaubheit, Arch. f. Psychiat. **32**:86, 1900.

16. Schilder, P.: The Localization of the Body Image (Postural Model of Body), A. Research Nerv. & Ment. Dis., Proc. **13**:466-484, 1932; The Image and Appearance of the Human Body, Psyche Monograph Series, no. 4, London, Kegan, Paul, Trench, Trubner & Co., Ltd., 1935, p. 353.

to minimize it. One must lead him back in this respect to reality. The basic trend in modern psychotherapy is to insist on truth. The aim is to bring the patient to a full appreciation of his attitudes and to enable him thus to see the situation clearly.

It is indispensable in the treatment of organic disease to bring the patient to insight into the reality of the disease and its character. Lack of appreciation of the disease and the experience of health is in many cases dangerous, as is emphasized particularly in the case of the patient with pneumonia who loses in delirium insight that he is sick and acts accordingly. The adaptation of the patient to his disease must be adaptation based on insight. When he has insight, the organic nature of the disease will keep it in the periphery. The patient has a right to know the nature of his disease, its cause and the diagnosis made.[17] Pain and anxiety call for the physical aid of the physician. The other part of therapy must be causal and not symptomatic. One has the right to let a patient maintain his experience of health only in the case of a serious physical ailment that is incurable. Then he may project his ailment and regress to a state of narcissistic bliss. This is also the answer to the problem of euthanasia. Incurable illness leads the sufferer away from the experience of disease to the experience of health and well-being. It is true that he regresses deeply. However, he still lives fully, and there is no more reason to kill the physical sufferer than a child. The psyche maintains the experience of health, even in the face of death.

SUMMARY

If serious disease threatens a person, he still tries to maintain the experience of health by minimizing the organic discomfort or by neglecting it completely. Organic disease lies not in the center of the personal life but in the periphery. Patients with organic disease are generally much more objective toward the disease than are those with psychogenic illness. Organic disease is in the periphery of the personality; psychogenic disorder occupies its center. Psychic life is a continuous movement of experiences from the center to the periphery and back. Patients with severe organic disease escape suffering by regression. The regression revives infantile love relations and passes finally to the oral stage. The experience of health can be maintained by the mechanism of projection. So-called psychogenic symptoms are common in organic disease. Appreciation of organic disease varies according to the general state of mind. Organic stimuli of minor degree may be the nucleus of conversion symptoms or may be used according to the general attitude of the sub-

17. It would be interesting to study morphine from the point of view emphasized here. The drug does not create anything new but merely reenforces the psychologic tendencies which drive to painlessness and ease.

ject. Organic symptoms of severe degree are never, and cannot be, without relation to the problems of the personality.

Noncortical lesions may aid in the experience of health. There is an undoubted relation between the Wernicke region and the experience of health. The experience of health and disease, although an attitude of the personality, is dependent on the function of specific centers in the brain, among which the Wernicke region is the most important.

Knowledge of the attitudes in organic and psychogenic diseases is of great diagnostic importance. It is indispensable in the treatment of the patient with organic disease to bring him to insight into the reality of the disease and its character. One has the right to allow the patient to maintain his experience of health only in the face of incurable physical ailment.

STRUCTURE OF THE NERVE ROOT

II. DIFFERENTIATION OF SENSORY FROM MOTOR ROOTS; OBSERVATIONS ON IDENTIFICATION OF FUNCTION IN ROOTS OF MIXED CRANIAL NERVES

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In a previous study [1] the structure of a typical cerebrospinal nerve root was investigated. The present study is concerned with the difference in structure of the various cerebrospinal nerve roots. Such a study has enabled the formulation of criteria for differentiating sensory and motor nerve roots. As a result, it has been possible to establish some degree of correlation between the structure and the function of certain roots of the mixed cranial nerves.

HISTORICAL REVIEW

That nerve roots vary with respect to the length of their glial segments has been recognized since the discovery of neuroglia. Virchow [2] called attention to the occurrence of neuroglia along the acoustic nerve. Henneberg and Koch [3] demonstrated a neuroglial extension constituting the central part of all nerve roots except the olfactory and the optic. It will be seen later that, like subsequent investigators, Henneberg and Koch were in error in their conception of the olfactory nerve in this respect. Henschen [4] and Lhermitte and Klarfeld [5] as well as Alexander

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From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

A part of this investigation was carried out in partial fulfilment of the requirements for the degree of Master of Science at McGill University.

1. Tarlov, I. M.: Structure of the Nerve Root: I. Nature of the Junction Between the Central and the Peripheral Nervous System, Arch. Neurol. & Psychiat. **37**:555 (Feb.) 1937.

2. Virchow, R.: Cellular Pathology, translated by F. Chance, London, J. & A. Churchill, Ltd., 1860.

3. Henneberg and Koch, M.: Ueber centrale Neurofibromatose und die Geschwülste des Kleinhirnbrückenwinkels (Acusticusneurome), Arch. f. Psychiat. **36**:251, 1902.

4. Henschen, F.: Zur Histologie und Pathogenese der Kleinhirnbrückenwinkeltumoren, Arch. f. Psychiat. **56**:20, 1915.

5. Lhermitte, J., and Klarfeld, B.: Gliome pré-protubérantiel avec métastases: Hémiplégie sans dégéneration du faisceau pyramidal, Rev. neurol. **21**:392, 1911.

and Obersteiner [5a] traced the neuroglial ensheathement of the two branches of the acoustic nerve as far as the plane of the internal acoustic meatus. Skinner,[6] in investigating some of the cranial nerves of man, pointed out that the glial outgrowth extends along certain sensory nerves farther than along motor nerves. Considering the olfactory tract and the optic nerve in the same category as the true cerebrospinal nerves, Skinner proposed the generalization that sensory nerves contain greater glial segments than motor nerves. It is unfair to introduce the olfactory tract or the optic nerve into the comparison, as they are integral fiber tracts of the brain rather than true nerves. Skinner's generalization was based entirely on the well known sensory fifth and eighth nerves. It was therefore premature, as several cranial nerves, as well as all the spinal nerves, were omitted. There was, moreover, no attempt to separate the sensory from the motor roots of the mixed nerves.

MATERIAL AND METHOD

Human material was used exclusively in this investigation. Information concerning the procedure employed in this study may be obtained in an earlier article.[1]

OBSERVATION

A. Comparison of the Cerebrospinal Nerves with Reference to Their Connective Tissue Framework and the Length of their Central Glial Segments.—The amount of glial outspread varies considerably not only among the different cerebrospinal nerves (fig. 1) but among the various rootlets of the same nerve. The glial segment increases in length from birth to adult life. It presents certain variations in persons of the same age and may differ on the two sides of the same person. In general, the length of the glial segment is directly related to the body length, yet considerable variations among persons of the same body length have been observed to exist (3 mm. in the case of the acoustic nerve). No constant differences between the sexes among subjects of the same height could be determined.

Any measurement of the glial outspread depends on the plane of section with reference to the nerve and its angle in relation to the brain. Furthermore, as the transition zone is helmet shaped, the point along its central concavity intersected by the section will determine to a great extent the measurement obtained. This factor, hitherto neglected, accounts largely for the discrepancies in the measurements of the central segments of the cranial nerves by various authors. The sources of error were minimized in this study to a certain extent by sectioning

5a. Alexander, G., and Obersteiner, H.: Das verhaltendes normalen Nervus cochlearis im Meatus auditorius internus, Ztschr. f. Ohrenh. **55**:78, 1908.

6. Skinner, H.: Some Histologic Features of the Cranial Nerves, Arch. Neurol. & Psychiat. **25**:356 (Feb.) 1931.

parallel to the course of the nerve fibers and well toward the center of the nerve and by averaging the results for many specimens.[7] In the following account of the cerebrospinal nerves the expression "transition dome" is used to indicate the central concavity bounded centrally by glia

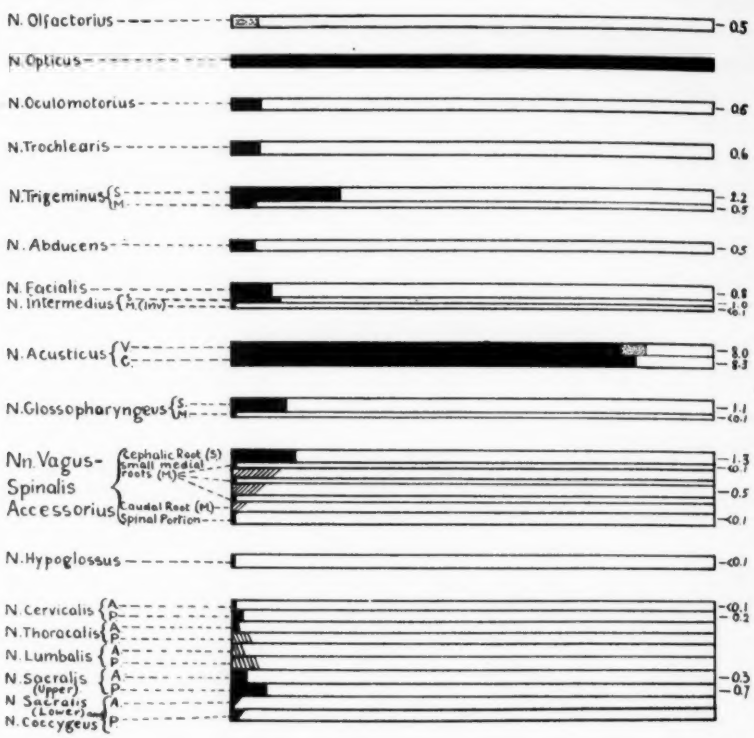

Fig. 1.—Diagram illustrating the length, expressed in millimeters, of the central glial segments of the cerebrospinal nerve roots. The sign < indicates that the measurement is usually less than the figure given, the corresponding nerve frequently lacking an appreciable glial segment. The central segment of the olfactory nerve is represented by dots rather than by a solid black area to indicate that it is variable in length, being often considerably smaller than is recorded. Stippling on the terminal portion of the vestibular area indicates that its glial segment may be greater or less than that of the cochlear division of the acoustic nerve. Hatched areas in relation to the vagus-spinal accessory complex indicate that the glial segment decreases in length gradually from the cephalic to the caudal roots. Hatched areas in relation to spinal roots indicate a gradual increase in length of the glial segments.

This drawing and the drawings in figures 3 and 4 were made by Miss F. Bechman.

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7. The brains of over fifty adults were examined in the course of this investigation, but complete sets of cranial nerves were not obtained in each instance. The number of nerves of different subjects on which the average measurement of the length of the glial segment is based is not less than ten in any case.

and peripherally by Schwann cells and endoneurium. It extends from the apex of the transition arch laterally to the termination of the pial ring, i. e., the approximation of the two pial layers. The lengths of the glial segments of the cerebrospinal nerve roots as indicated in the diagram represent the averages. Variations of from one-third to three times the measurements indicated have been encountered in all nerves except the eighth. The height of the transition dome varied up to 1 mm. (in the sensory division of the trigeminal nerve). It is greater usually on the larger nerve roots.

The olfactory nerve presents an appearance quite different from that of the other cerebrospinal nerves and must be considered apart. The connective tissue of the nerve, projecting centrally, penetrates the bulb, incompletely dividing its fiber layer by septums of fine reticulin. As the nerve is followed from the bulb toward the cribriform plate, the septums assume the form of more definite sheaths. These sheaths are at first large and plexiform. They contain bundles or a network of nerve fibers, finally converging to form more compact trunks containing a fairly characteristic endoneurium of longitudinal fibers and a delicate interlacing web. These compartments of connective tissue differ from those of the true cerebrospinal nerves in presenting a less orderly parallel arrangement and in being of less uniform size. Moreover, these sheaths subdivide and anastomose, in contrast to the usual more independent nature of the Plenk-Laidlaw argyrophilic sheaths of the other cerebrospinal nerves. The olfactory nerve must be considered, therefore, as possessing a central glial and a peripheral nonglial portion (fig. 2 *A*). It is difficult to fix the exact point of transition on this nerve in view of the diffuseness of the endoneurium at its origin and the ill defined nature of the pial ring. The approximate length of the central glial segment of the olfactory nerve is taken as 0.5 mm.,[8] some of the roots, however, lacking at times an appreciable glial segment.

The optic nerve represents a fiber tract of the brain and therefore cannot be divided into a central and a peripheral portion. Within the nerve a connective tissue structure, aside from that of the vessels, first appears just anterior to the chiasm. Here pial septums pass inward to divide the nerve into bundles of unequal size. The nerve, of course, lacks an endoneurium (fig. 2 *B*).

The glial segment of the facial nerve presents considerable variation in length, owing to a not infrequent peculiarity in the disposition of the dome of transition. While the apex of this glial dome is usually in the

8. This measurement represents the distance from the olfactory bulb to the point along the nerve at which its reticulin assumes more or less the pattern of well defined endoneurial compartments. It is in this region approximately that the neuroglia has been observed to disappear, Schwann cells and other peripheral ensheathing cells covering the nerve fibers.

center of the trunk, its border may reach the site of origin of the nerve from the brain, instead of terminating distal to the point of upward pial reflection. In other words, the height of the concavity of the transition dome may be the same as the length of the glial segment. Hence, sections taken at the periphery of the nerve trunk may show a very slight glial segment and others passing through the center of the glial dome a very long one. The upper limit of measurement encountered for the glial portion was 2 mm., ending in a glial tongue of 1 mm. projecting

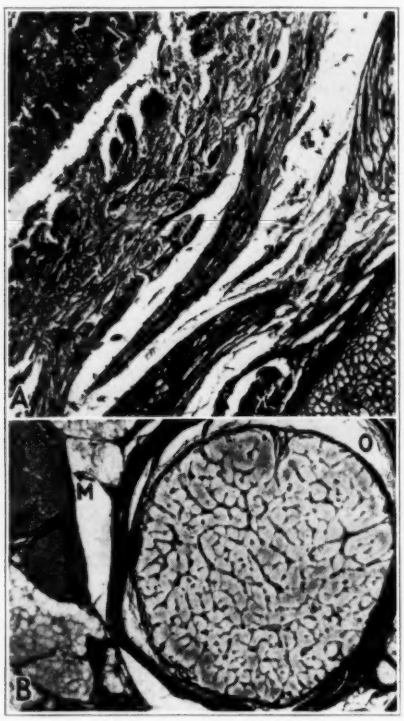

Fig. 2.—Photomicrographs (× 100) of nerves impregnated with lithium silver carbonate (Laidlaw's modification of Río-Hortega's technic for connective tissue). *A* shows a section of the olfactory nerve roots, with diffuseness of the endoneurium and the ill defined nature of the transition from the central to the peripheal nerve segment, and *B*, the structure of the connective tissue of the optic nerve (*O*) and the oculomotor nerve (*M*), with the absence of endoneurium in the optic nerve.

farther peripherally. Usually, however, the glial segment does not exceed 0.8 mm., the dome occupying approximately one half of this distance. The two types of intermedius roots present the contrasting features of the anterior and the posterior spinal root. A root of type 1 arises as a main stem, without presenting the split appearance of the more delicate root of type 2 (fig. 3).

The anterior (cephalic) medial portion of the eighth nerve represents the vestibular component, the cochlear division occupying a posterior lateral position. The roots are closely united, a sulcus marking the division. An additional groove may indicate a further splitting of one or the other component. The transition site, usually at the plane of the porus acusticus internus, may occur either central or peripheral to

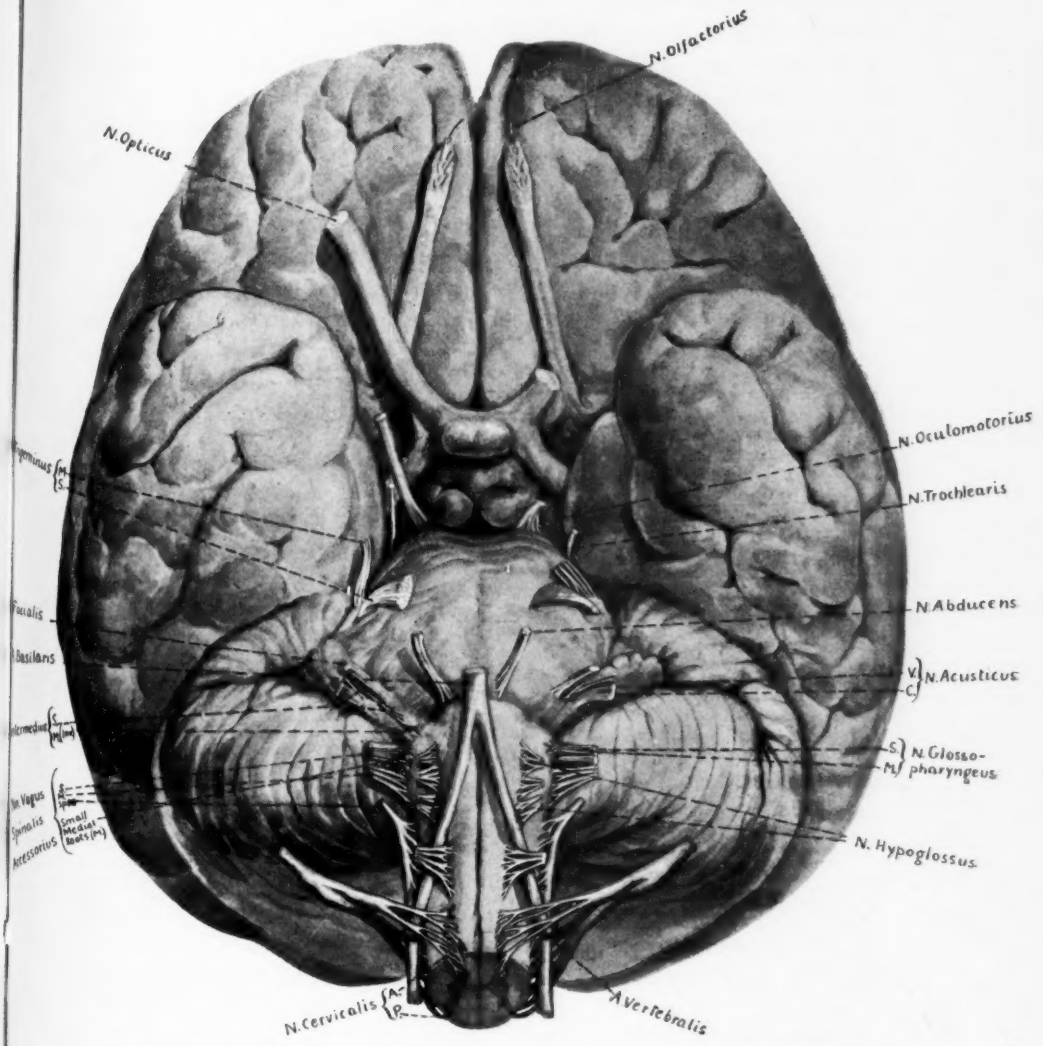

Fig. 3.—Drawing of the cerebral and first cervical nerve roots. The differences in the nerve roots of the nervus intermedius, the glossopharyngeal nerve and the vagus-spinal accessory complex are emphasized for clarity. The resemblance in the bifurcation of the smaller roots of these nerves to that of rootlets of the anterior spinal root is evident. Varying degrees of approximation and even of fusion of these roots may occur.

it, the limits of the glial length being 5 and 11.5 mm. The length of the glial segments on the two divisions of this nerve may vary within 1.2 mm. In thirteen of eighteen specimens examined the glial portion of the cochlear division exceeded in length that of the vestibular, the vestibular glial portion being longer in three instances and no difference occurring in the remaining two. The dome of transition from its apex to its lateral termination in the pia averaged 1.1 mm.

The posterior spinal roots are large, usually presenting a pial constriction [9] at their emergence, most marked ventrolaterally. The transition from the central to the peripheral nerve segment is arched, the dome in the case of the posterior cervical roots occupying as much as 0.4 mm. at times and the glial segment being of the same length or slightly greater. The peripheral root fibers may undergo transition of their sheaths at or slightly below the internal pial layer. For this reason, sections along the periphery of the root indicate a transition in the form of a straight line. Usually, however, an arch exists. In the cervical segments the anterior rootlets present a transition zone in the form of practically a straight line parallel or slightly oblique to the main axis of the spinal cord. This takes place usually at the internal pial layer or distinctly within the substance of the cord, the intima pia passing inward to give rise to the pial ring (fig. 4).

The remaining spinal roots are constructed on the same general plan. The obliquity of the roots increases caudally. In addition, there is a tendency for the site of transition to migrate peripherally from the upper to the lower spinal roots. In the lumbar and upper sacral posterior roots the length of the glial segment, averaging 0.7 mm., exceeds the height of the transition dome. The pial constriction occurs central to the zone of transition. One lateral border of the glial segment may contain pia and the other endoneurial sheaths, as anteriorly. The endoneurial border occurs at the acute angle, indicating that the upper (cephalic) border is subject to a greater degree of tension during the period of unequal growth of the spinal cord and the vertebral column. In the lumbar and upper sacral anterior roots a similar, though less striking, peripheral migration of the transition zone has occurred. While the upper sacral roots conform in thickness and in the length of their glial segment to the lower lumbar roots, those of the lower sacral segments approach the coccygeal roots in being slender and having a short glial segment.

9. The cranial nerves differ from the usual spinal nerves in lacking a pial constriction in the region of their emergence from the central axis. The cranial nerves may, however, present a slight bulging beyond the point of superficial origin, usually in the zone of transition.

As a general rule it may be stated that the transition zone occurs intraspinally in the cervical segments,[10] below the site of pial constriction. In the lumbar and upper sacral roots the transition is extraspinal, occurring distal to the site of pial constriction. The lower sacral and coccygeal roots approach the cervical roots in this respect. In the intermediate segments, evident in the lower thoracic regions particularly, the transition zone and the site of pial constriction may coincide. These facts were pointed out in part by Obersteiner and Redlich [11] with respect to the posterior roots and were confirmed and amplified by Levi.[12] While it may often be true, it must be understood that the outward shift of the transition zone is gradual and that differentiation of roots in the various spinal segments on the basis of the site of the pial constriction and the transition zone is not reliable, since exceptions are numerous.

Fig. 4.—Diagram illustrating intramedullary transition along a nerve root. Such a transition may occur along certain spinal roots (particularly the anterior roots of the higher spinal nerves), the roots of the hypoglossal nerve and the small bifurcated roots of the nervus intermedius, the glossopharyngeal nerve and the vagus-spinal accessory complex. In the case of the spinal nerves the transition site occurs more distally on the posterior than on the anterior roots; the pial constriction is more marked on the posterior roots also. The transition site becomes increasingly peripheral as one passes caudally along the spinal roots. In the more caudal of the spinal roots the transition site is extramedullary, the inner layer of the pia passing upward to give rise to the pial ring rather than dipping into the neural axis, as in the case of the intramedullary transition represented.

The cells and connective tissue of the nerve roots are somewhat greater in amount for a given area on the sensory than on the motor

10. An intraspinal transition occurs less commonly in the case of the posterior than in that of the anterior roots.

11. Obersteiner, H., and Redlich, E.: Ueber Wesen und Pathogenese der tabischen Hinterstrangsdegeneration, Arb. a. d. Inst. f. Anat. u. Physiol. d. Centralnervensyst. an d. Wien. Univ., no. 2, 1894, p. 158.

12. Levi, E.: Studien zur normalen und pathologischen Anatomie der hinteren Rückenmarkswurzeln, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **13**:62, 1906.

roots. Similar, although less striking, differences are manifest in comparisons of the most cephalic with the most caudal of the vagus-spinal accessory roots, the amount of cells and connective tissue favoring the former group. The smaller medial roots of this complex, like those of the glossopharyngeal nerve, regarded as motor roots on the basis of their short glial segment, are an exception in that their reticulin fibers, although delicate, are closely ranged. Their cells similarly appear more numerous for a given area than those in the usual motor roots. While the roots of the nervus intermedius contain a greater number of cells and more of a reticulin framework than the root of the main facial trunk, no differences between the two types of intermedius roots could be detected. The individual endoneurial fibers are usually greater on the large-fibered nerves. In the premature and the full term infant the cells of the nerves occupy a more predominant position than in adults. The growth of the nerve fiber is probably responsible for this apparent cellular decrease with age. In young subjects the endoneurial tubes are narrower and their collagen fibers less well developed.

In the eighth nerve the cells and connective tissue may appear somewhat more in amount on the cochlear than on the vestibular division, the cochlear division presenting a greater number of fine nerve fibers. Although differences in the degree of cell piling at the transition zone frequently appear, no constancy in the division favored could be determined.

B. Criteria for the Differentiation of Sensory and Motor Roots.—Grossly motor nerves differ from sensory nerves in consisting of smaller, less compactly spaced filaments at their respective sites of origin (fig. 3). This is exemplified in the spinal cord, particularly in the upper cervical region. The sensory roots possess in general a longer glial segment than the motor roots (fig. 1). This rule does not apply in a comparison of the cerebral and the spinal roots, as certain motor cerebral roots contain a longer glial segment than certain sensory spinal roots, Similarly, in the spinal cord motor roots at one level (e. g., the lumbar) may exceed in the length of their glial segment the sensory roots at another level (e. g., the cervical). The rule usually applies to the cerebral roots as a group[13] and is most applicable to the roots of a given segment (figs. 5, 6 and 7). The sensory roots are usually richer in cells constituting both the central and the peripheral portion and similarly contain more connective tissue fibers than the main motor roots. As the size of the nerve fiber seems to be the conditioning factor in the amount of connective tissue and in the number of cells

13. The olfactory nerve is frequently an exception in presenting a shorter glial segment than many motor nerves. It differs from other cerebrospinal nerves in being more primitive in the organization of its nerve fibers and interstitial substance.

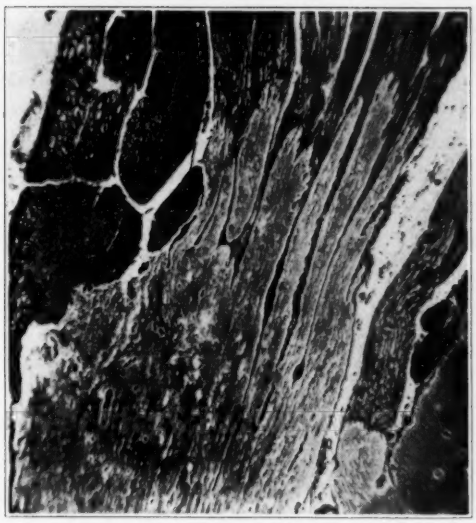

Fig. 5.—Photomicrograph of a section of the trigeminal nerve, showing the difference in the length of the glial segment on motor (at the right) and on sensory roots. Impregnation with lithium silver carbonate (Laidlaw's modification of Río-Hortega's technic); × 115.

Fig. 6.—Photomicrograph of a section of glossopharyngeal nerve roots. The short glial segment of the small roots (ventral to the large root) is compared with the long glial segment of the main root. The splitting of the pia mater (on the left) gives rise to the pial ring and the outermost layer of the endoneurium. Impregnation with lithium silver carbonate (Laidlaw's modification of Río-Hortega's technic); × 70.

occurring in the nerves, in inverse proportion, one encounters motor roots containing fine nerve fibers which present an exception to this rule. At the transition zone of the nerve root a piling up of cells occurs. This phenomenon is, as a rule, more conspicuous on the sensory than on the motor roots (fig. 8 *A* and *B*).

C. Localization of Function in the Roots of the Mixed Cranial Nerves.—The glial peculiarities of the sensory and motor roots offer a means for their differentiation in the mixed cranial nerves. The motor roots of the trigeminal nerve may thus be easily distinguished from the sensory roots. The motor roots contain a shorter glial segment (fig. 5), fewer interstitial cells and less connective tissue, with little evidence of cell piling at the transition zone. The cellular increase at the border and the long glial segment in the sensory root are usually striking. The accuracy of this standard of differentiation in this

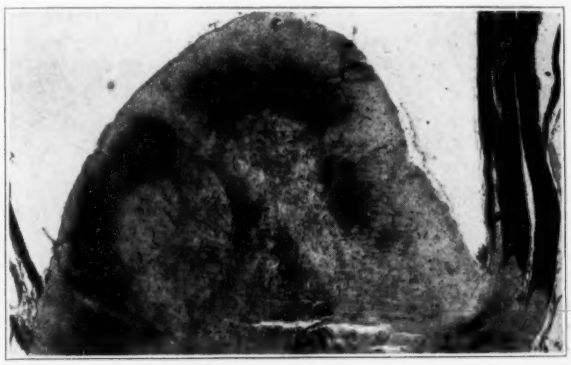

Fig. 7.—Photomicrograph of a portion of the cervical part of the spinal cord. The length of the central segment on the anterior (left) and the posterior root are compared. The central segments are longer than normal, since the cervical portion of the cord was dislocated downward as a result of hydrocephalus, with resulting elongation of the nerve roots. Unsuccessful myelin sheath stain; × 38.

instance may be demonstrated by a study of the characteristics of the nerve fibers. On the basis of the latter the motor roots may be identified by the presence of greater numbers of large efferent fibers and few of the fine fibers which predominate in the sensory component.

The differential criteria offered assume greater interest in the case of the seventh nerve. The series of rootlets comprising the nervus intermedius of Wrisberg is composed of two types. The two types of rootlets are often in contrast grossly, as are those of the sensory and motor spinal nerves (fig. 3), the latter being composed of finer filaments undergoing characteristic splitting at their emergence. Microscopically the roots present fairly constant differences. The larger cephalic root (fig. 9 *B*), at times several, presents a longer glial segment, with evi-

Fig. 8.—Photomicrographs (impregnation with silver carbonate; × 115): (*A*) of the posterior lumbar root, showing the greater central segment and the more intense cell piling than in the anterior root, and (*B*) of the anterior lumbar root, showing the greater length of central segment than in the anterior cervical root.

Fig. 9.—Photomicrographs showing oligodendrocytes (*A*) along the main motor root of the facial nerve, and (*B*) along the main (nonbifurcated) root of the nervus intermedius, on which the glial segment is longer and the cell piling more intense than on the other roots of this nerve. Impregnation with silver carbonate (modification of Río-Hortega's technic); × 135.

dence usually of greater heaping up of cells at the site of transition than in the smaller, more caudal roots (fig. 10). These roots may arise well along the vestibular trunk, in which case they may be differentiated from branches of the vestibular nerve by the predominance of fine nerve fibers in the former and, consequently, the occurrence of small ensheathing cells (oligodendrocytes and Schwann cells), the interstitial cells being therefore more numerous. The gross and miscroscopic morphologic features of these two types of roots suggest a segregation of the nervus intermedius into sensory and motor components. That the motor components of the nervus intermedius may in some cases undergo a further segregation into separate roots containing the vasodilator and glandular secretory fibers is possible, as a series of rootlets sometimes constitutes the type 2 portion. Further studies of nerve fibers and their central connections may contribute toward a solution of this problem. The large motor facial root may be readily distinguished from roots of the other two types. It differs from the true sensory portion in containing ordinarily a shorter glial segment. The fact that it contains at times a longer glial portion than the sensory root is probably an expression of the tendency on the part of this nerve to assume an increasing importance, eclipsing the sensory portion in phylogenetic significance. The main motor root (fig. 9*A*) exhibits little of the cellular increase at the border of the sensory root (fig. 9*B*). It differs from the smaller roots of the nervus intermedius (fig. 10) in the greater length and diameter of its glial segment. Its fairly thick motor fibers, like those of the motor fifth nerve, differ strikingly from the predominating fine fibers of the roots of the nervus intermedius. The intermedius roots contain more interstitial cells, which are for the most part smaller than those of the main motor root.

In the ninth nerve a certain amount of segregation of the roots similarly occurs. The finer ventral rootlets conform in glial structure to the smaller motor rootlets of the nervus intermedius, presenting a short glial segment with little evidence of cell piling at the border. The main trunk contains a relatively long glial segment, exhibiting heaping up of cells at the transition zone. It is therefore characteristic of a sensory root. A root intermediate in position and structure may occur. On this basis it seems justifiable to assume that the glossopharyngeal nerve contains a dorsal trunk which is chiefly sensory and one or more small ventromedial rootlets of motor type (fig. 6.) Differences in the constitution of the nerve fibers of these two types of roots were not impressive. The lateral (dorsal) roots of the vagus-spinal accessory complex are thick, and the more cephalic roots are usually accompanied by smaller medial rootlets. These ventromedial filaments correspond to those of the glossopharyngeal rootlets and those of the caudal portion of the nervus intermedius, presenting a short glial seg-

Fig. 10.—Photomicrograph showing oligodendrocytes along small (bifurcated) rootlets of the nervus intermedius. The short glial segment and slight cell piling at the transition zone are evident. These rootlets resemble those of the anterior spinal nerves and the small ventral rootlets of the glossopharyngeal and vagus nerves. Impregnation with silver carbonate (modification of Río-Hortega's technic); × 135.

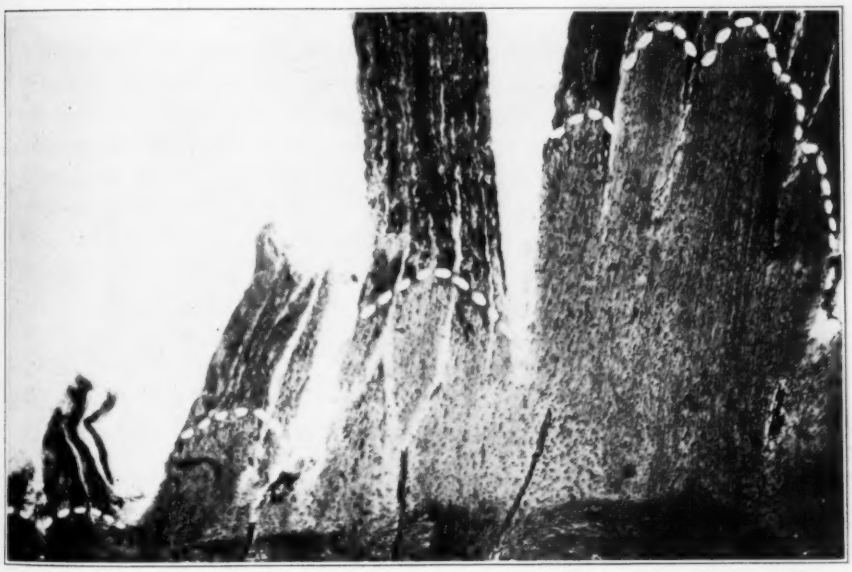

Fig. 11.—Photomicrograph of the vagus-spinal accessory complex, showing the decreasing length of the glial segment caudally. Impregnation with silver carbonate (Río-Hortega's technic for astrocytes); × 27.

ment with little or no cellular increase at the border; they seem, therefore, to be motor. They are separated by variable distances from the main trunk and may fuse with it. No constant differences in the number and size of the interstitial cells of the medial and lateral roots were detected.

Section through the main roots of the vagus-spinal accessory complex reveals that the glial segment decreases caudally (fig. 11). The anterior or cephalic vagus roots contain long glial segments and usually moderate cell piling at the transition zone. The spinal roots of the eleventh nerve are for the most part [14] similar to the anterior roots of the spinal nerves, their glial segments being short and the cells undergoing little increase at the border zone. Between these two types of roots the transition is gradual. The more caudal of the large roots of the vagus series contain a glial segment measuring one-half or less that of the cephalic, clearly sensory roots. The conclusion follows on the basis of the glial criteria that the main cephalic portion of this complex is predominantly sensory and the caudal portion chiefly motor, the smaller ventral roots of the complex being likewise of the motor type.

COMMENT

The gross difference between sensory and motor roots is exemplified in the spinal roots of the upper segments particularly, where the posterior roots enter the cord as large rootlets and the anterior roots emerge as a series of fine filaments (fila radicularia), which later coalesce to form rootlets. Similar differences usually exist among the various rootlets of the nervus intermedius of Wrisberg and of the trigeminal, glossopharyngeal, vagus and spinal accessory nerves. These dispositions seem to be the result of differences in development of the sensory and the motor roots. While the former develop from the ganglionic crest, growing centripetally and entering the neural axis as a compact bundle or as a series of such bundles, the motor roots emerge from the neural axis as the filaments of ganglion cells located at appreciable distances from each other, becoming more closely associated only farther peripherally. In other words, a nerve at its origin exhibits its constituent filaments, which well along its course or near its termination are more closely associated. In the case of the sensory root at the level of the brain or spinal cord one approaches the termination of the nerve. The corresponding site on the motor nerve represents, on the contrary,

14. The fact that one encounters among the spinal portion of the eleventh nerve roots which resemble grossly and microscopically the posterior cervical roots makes it likely that this nerve may contain a sensory component. The predominating pattern of the spinal portion of the eleventh nerve roots, however, conforms to that of the motor roots.

the nerve origin—hence, the difference grossly between the sensory and the motor roots.

The fact that the glial segment of the sensory roots exceeds in length that of the motor roots is probably explained on the basis of differences in the source of the peripherally ensheathing Schwann cells. In the case of the sensory root the neural crest or the placode is the sole origin of these cells. In addition to this source, the cells of the motor root are derived, to a less extent, from the medullary tube. Such migration of medullary cells forming sheath cells has been observed by Neal [15] and, to a less marked degree, by Carpenter and Main,[16] Harrison,[17] Van Campenhout [18] and others. The central as well as the peripheral origin of the sheath of Schwann cells of the motor root might tend, therefore, to provide greater peripheral ensheathement and, hence, less glial ensheathement (i. e., shorter central segments) than those of the sensory root.

The increase in the glial segment of the spinal nerves caudally probably results from tension exerted on the nerve roots by the relatively unequal rates of growth of the spinal cord and the vertebral canal, the spinal ganglia being relatively fixed at their respective intervertebral foramina. The maximum effect of such a stretch is exerted on the lumbar and upper sacral roots, the lower sacral and coccygeal roots being smaller and less firmly anchored in the region of their intervertebral foramina. The variation in the length of the glial segment of the different cranial nerves may be related to a time factor in the development of these nerves and to spatial relationships existing between the neural crest and the superficial origin of the nerve trunks which it supplies.

The tendency toward a piling up of cells at the transition zone is greater in the sensory than in the motor roots, often being lacking in the latter. Only to a slight extent does the inequality of appearance on the sensory and the motor roots result from the greater number of cells usually occurring along the sensory root. The appearance of cell piling at the transition site is due, to a certain extent, to the presence of the marginal neuroglial layer bridging the nerve root in this zone, the cells of the connective tissue reenforcement of the pial ring accentuating the effect. In addition, however, there is usually a real tendency toward heaping up of cells in this region. The greater cell piling

15. Neal, H.: Morphology of the Eye Muscle Nerves, J. Morphol. **25**:1, 1914.

16. Carpenter, F., and Main, R.: Migration of Medullary Ceils into the Ventral Nerve Roots of Pig Embryo, Anat. Rec. **1**:63, 1906-1907.

17. Harrison, R. G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, J. Comp. Neurol. **37**:123, 1924-1925.

18. Van Campenhout, E.: Contribution to the Problem of the Development of the Sympathetic Nervous System, J. Exper. Zoöl. **56**:295, 1930.

at the transition zone in the sensory root seems to be dependent on developmental factors. In this case the ensheathing elements of the central glial and the peripheral nonglial segment are opposite in direction of growth; that is, the one proceeds centrifugally and the other centripetally. It is possible that in the case of the motor root the lesser, accessory centrifugal, as well as the centripetal, source of the Schwann cells, providing opportunity for mutual adjustment between the neuroglia and the Schwann cells before their encounter at the transition zone, moderates the violence of the interaction. That these opposing cell currents may produce a reaction is indicated by the diminution or absence of the phenomenon of cell piling when glial tongues or glial islands occur peripherally along a nerve root. A lessened intensity of reaction, therefore, seems to occur when the glial cells are not entirely thwarted at the transition zone.

The differences in sensory and motor roots, illustrated in the spinal nerves, are borne out by examination of the cranial nerves, particularly the roots of the fifth, seventh, ninth, tenth and eleventh nerves. Segregation of certain components in specific roots of these nerves can be understood in view of the distinct positions of their respective nuclear masses in the brain stem. The occurrence of two distinct motor portions of the vagus-spinal accessory complex, the one contained in the small ventral roots and the other in the large caudal roots, seems to be specifically related to the two components of these nerves, the one belonging to the special visceral efferent and the other to the general visceral efferent system. Streeter,[19] on the basis of embryologic studies, concluded that the vagus-spinal accessory complex undergoes differentiation into a forepart, predominatingly sensory, and a hindpart, chiefly motor. This is in agreement with the conclusion reached by Chase and Ranson [20] and Foley and Du Bois [21] on the basis of studies on nerve fibers. Similar deductions were made by van Gehuchten and Molhant.[22]

SUMMARY

The length of the central glial segment varies on the different cerebrospinal nerves. The eighth nerve presents the longest glial segment, either the vestibular or the cochlear division excelling. Among the

19. Streeter, G.: The Peripheral Nervous System in the Human Embryo at the End of the First Month, Am. J. Anat. **8**:225, 1908.

20. Chase, M., and Ranson, S.: The Structure of the Roots, Trunk and Branches of the Vagus Nerve, J. Comp. Neurol. **24**:31, 1914.

21. Foley, J., and DuBois, F.: Experimental and Anatomical Studies on Vagus Nerve of Cat, Proc. Soc. Exper. Biol. & Med. **30**:571, 1933; An Experimental Study of the Rootlets of the Vagus Nerve in the Cat, J. Comp. Neurol. **60**:137, 1934.

22. van Gehuchten, A., and Molhant, M.: Contribution a l'étude anatomique du nerf pneumogastrique chez l'homme, Névraxe **13**:55, 1912-1913.

spinal nerves the glial segment increases as one descends the spinal cord to the lumbar and upper sacral region, from whence it decreases to the coccygeal roots. The sensory nerves possess in general a longer glial segment than the motor nerves. This generalization applies more strictly to the roots of a given segment. The sensory roots are usually richer in cells constituting both the central and the peripheral portion and contain more connective tissue fibers than the main motor roots. The phenomenon of cell piling is usually more conspicuous on the sensory than on the motor roots. Grossly the motor roots differ from the sensory in consisting of smaller, less compactly spaced filaments at their respective sites of origin.

These various differences between sensory and motor nerves, the most important criterion of which is the length of the glial segment, enable one to differentiate the sensory from the motor roots of the mixed nerves. They permit a certain degree of functional localization in the roots of the nervus intermedius and the ninth, tenth and eleventh cranial nerves. In the case of the nervus intermedius it seemed justified to assume that the sensory and motor components at their superficial origin are contained in separate rootlets. On the basis of the criteria offered, the ninth, tenth and eleventh nerves contain small ventral rootlets, motor in type. In addition, the anterior portion of the vagus-spinal accessory complex is chiefly sensory and the posterior (caudal) portion predominantly motor.

CONCLUSIONS

Motor nerves differ grossly from sensory nerves in being composed of a greater number of fine filaments at their superficial origin. Microscopically the sensory roots contain longer glial segments than the motor roots, the latter usually being less cellular and exhibiting to a less extent the phenomenon of cell piling at the transition zone.

On the basis of these criteria, the nervus intermedius of Wrisberg is a mixed nerve, usually containing separate motor and sensory roots. The involuntary motor roots are distinct from the main voluntary motor portion of the facial nerve.

The glossopharyngeal nerve usually contains separate motor and sensory roots.

The vagus-spinal accessory complex often consists of two distinct motor portions, the one contained in the small ventromedial roots and the other in the large caudal roots. The cephalic portion of this complex is chiefly sensory.

Varying degrees of approximation and even fusion of the rootlets of the nervus intermedius, glossopharyngeal nerve and vagus-spinal accessory complex may occur.

GANGLIOGLIONEUROMA OF THE SPINAL CORD ASSOCIATED WITH PSEUDOSYRINGOMYELIA

A HISTOLOGIC STUDY

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AND
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Of the intramedullary tumors of the spinal cord, true neuroma, consisting of ganglion cells, glia cells and large numbers of nerve fibers, is rare. Though common in the sympathetic nervous system, this tumor is rare in the cerebrospinal nerves, the spinal ganglia and the brain itself. Only one instance was reported by Foerster [1] in which such a tumor was restricted to the spinal cord. In two other cases the tumor extended from the medulla into the upper cervical portion of the spinal cord, reaching the second segment, in the case reported by Pick and Bielschowsky,[2] and the third segment, in that recorded by Foerster and Gagel.[3] Unfortunately, this tumor has been described under a variety of names, such as ganglionic neuroma, neuroglioma, ganglionic glioma, neuroganglioma and ganglioglioneuroma. The most commonly used term, ganglioneuroma, is inaccurate, in that it names only one of the cellular constituents of this tumor. Though the term ganglioglioma indicates the two essential types of cells, many authors prefer the term ganglioglioneuroma. Varied as the terminology is, the histologic structure of this nerve tumor is so characteristic that it forms an important and distinct type of neurogenic neoplasm.

Virchow [4] was the first to differentiate satisfactorily the true neuroma, containing newly formed nerve elements, from the large group

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From the Pathologic Laboratories (Dr. R. H. Jaffé, Director) of the Cook County Hospital, and the Division of Neuropathology (Dr. G. B. Hassin) of the University of Illinois College of Medicine.

1. Foerster, Augustin: Ein Ganglioneurom des Rückenmarks, Virchows Arch. f. path. Anat. **253**:116, 1924.

2. Pick, Ludwig, and Bielschowsky, Max: Ueber das System der Neurome und Beobachtungen an einem Ganglioneurom des Gehirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **6**:392, 1911.

3. Foerster, O., and Gagel, O.: Ein Fall von Gangliocytom der Oblongata, Ztschr. f. d. ges. Neurol. u. Psychiat. **141**:797, 1932.

4. Virchow, R.: Das wahre Neurom, Virchows Arch. f. path. Anat. **13**:256, 1858.

of false neuromas, in which such elements are absent. In our opinion, the classification of true neuromas elaborated by Pick and Bielschowsky [2] on an embryologic basis is satisfactory. These authors stated that the anlage of every true neuroma is a developmental defect in the embryo, with an abnormal deposition of multipotential embryonal neurocytes. Through the differentiation or lack of differentiation of these primitive cells, mature or immature forms of neuroma arise. To the latter (immature) group belong, in their opinion, neurocytoma and neuroblastoma, and to the former (mature) group, the ganglioglioneuroma, in which the multipotential neurocytes have differentiated into glia tissue, on the one hand, and ganglion cells and nerve fibers, on the other. Such features were present in the tumor to be described, which gave a clinical picture of slowly and progressively developing kyphoscoliosis.

REPORT OF A CASE

History.—A. R., a white man aged 20, entered the Cook County Hospital on Sept. 13, 1935, complaining of difficulty in urination for one and one-half years. It had become marked in the preceding two weeks and was accompanied by a burning sensation, periodic passage of blood and continuous dribbling. The patient stated that he had had infantile spinal paralysis when 3 years of age, followed by paralysis of the right leg and hump back. The deformity of the back had progressed to the state noted at the time of observation, and, in addition, there was pigeon breast. The family history was of no special significance. He had had a fracture of the left hip one and one-half years before.

General Examination.—On admission, the patient was moderately ill; the temperature was 103 F., the pulse rate 120, the respiratory rate 26 and the blood pressure 120 systolic and 80 diastolic. The outstanding physical findings were: marked thoracic dextrokyphoscoliosis, with compensatory lordosis of the lumbar region and rotation of the cervical vertebrae; pigeon breast; systolic murmur heard over the precordium; distention of the abdomen, with the fundus of the urinary bladder extending half-way to the umbilicus, and right talipes equinovarus.

Neurologic Examination.—The pupils reacted normally to light and in convergence and accommodation. The cranial nerves, speech and mental condition were also normal. Motor power in the upper extremities was good, and sensibility, as well as the deep tendon and periosteal reflexes, was normal. There was marked paraplegia in flexion of the lower extremities, with spasticity and resistance to passive motion. Painful stimulation of the lower extremities provoked powerful defense reflexes, in the form of spontaneous contractions. There were complete loss of the sensations of pain and temperature and partial loss of the sensations of touch up to the level of the nipples. Deep sensibility was preserved to a certain extent in the toes of the left foot but was absent elsewhere in both lower extremities. There was complete retention of urine and feces, with continuous overflow of the distended urinary bladder. The patellar reflexes were present bilaterally, but the achilles reflex could not be elicited. Whereas on the right side there were positive Babinski, Chaddock and Mendel-Bechterew signs, only Rossolimo and Mendel-Bechterew signs were elicited on the left. Both patellar and ankle clonus were absent bilaterally, as were the abdominal and cremasteric reflexes.

Clinical Diagnosis.—Compression of the spinal cord was indicated at the level of the sixth thoracic segment, with a "neurogenic" bladder and sepsis of the urinary tract. The type of compression could not be determined.

Laboratory Data.—The white cell count was 13,000 per cubic millimeter, with a normal differential rating. The Kahn reaction of the blood was negative. Chemical examination of the urine revealed a variable amount of albumin, and microscopic examination showed the presence of pus and occasional red cells.

A roentgenogram of the spine revealed only marked spinal curvature.

Course.—The temperature was of septic type, at times reaching as high as 104 F. The patient was acutely ill. Because of the spinal curvature, lumbar puncture was impossible, and cisternal puncture was deferred on account of the seriousness of the general physical condition. The urinary bladder was irrigated, and urinary antiseptics were administered. The condition grew worse; decubital ulcerations developed, and the patient died on October 26, six weeks after entering the hospital and more than one and one-half years after onset of the urinary symptoms.

Necropsy (Dr. A. B. Ragins).—The anatomic diagnosis was: ganglioglioneuroma of the thoracic portion of the spinal cord with pseudosyringomyelia; bilateral ascending pyelonephritis; hemorrhagic and pseudomembranous cystitis; catarrhal ureteritis and pyelitis; focal bronchopneumonia in the upper and the lower lobe of the right lung, and kyphoscoliosis.

Macroscopic Observations.—Except for the marked cystitis, ureteritis, ascending pyelonephritis and confluent bronchopneumonia in the upper and lower lobes of the right lung, the essential changes were in the spinal cord. Because of the spinal curvature and the limitations placed on the necropsy, only the portion of the spinal cord beneath the greatest convexity of the curvature could be removed without undue mutilation of the body.

When the spinous processes were removed, an enlarged dural sac, tightly bound to the left side of the spinal canal, was exposed. A jelly-like, xanthochromic fluid was discharged from the intermeningeal spaces when the dura and cord were severed at their upper and lower limits.

The portion of the spinal cord removed for microscopic study measured 11 cm. in length. Its consistency was markedly diminished. After being hardened in a 10 per cent dilution of formaldehyde, U. S. P., it was sectioned into segments 1 cm. long. The dura mater was greatly thickened, and the intermeningeal spaces were filled with a light yellow, colloid substance, which fused imperceptibly with the outer layers of the white matter. The average measurements of the cord were 18 mm. in the transverse diameter and 16 mm. in the anteroposterior diameter. The internal configuration was altered so severely that the normal segmental differentiation was impossible. Close inspection of the gross specimen revealed an intramedullary tumor at all levels.

In its uppermost portion (fig. 1, segment *1*, and fig. 2 *A*), the tumor was centrally placed, soft and light yellow brown. It contained a small central cavity, which was almost completely occluded by a solid, firm, gray-white nodule. At the lower levels (fig. 1, segment *4*, and fig. 3), the central cavity became much larger and occupied an eccentric position within the tumor, which was firm and grayish white. Below this level the middle segment of the spinal cord (fig. 1, segment *5*, and fig. 4) assumed the configuration of a hollow tube, and was lined with a layer of light yellow-brown tumor tissue, 2 mm. thick. In the most caudal por-

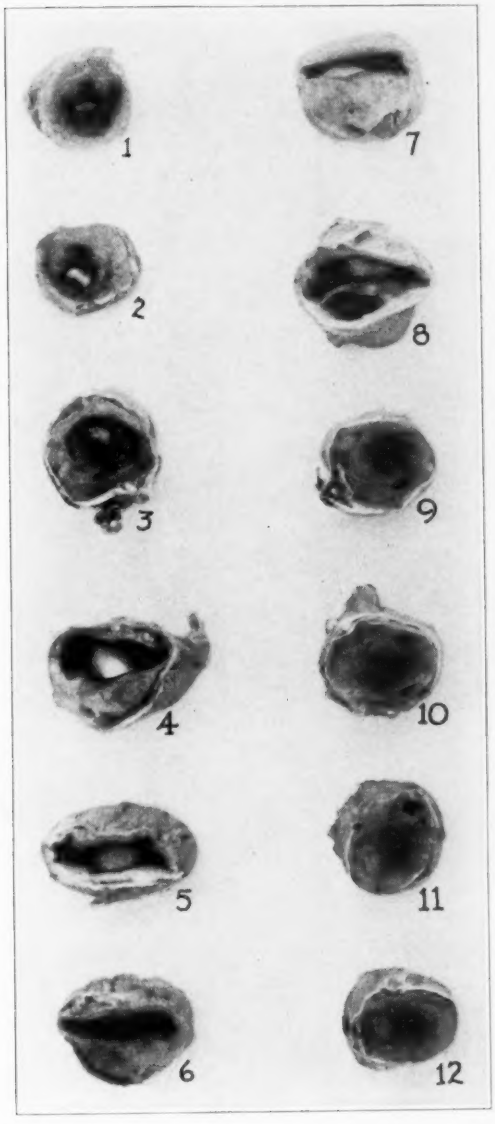

Fig. 1.—Photographs of unstained transverse sections of the spinal cord. Segments *1* and *12* are reproduced under higher magnification in figure 2 *A* and *B*, section *4* is shown in figure 3, and section *5*, in figure 4.

tions of the spinal cord (fig. 1, segments *10* and *11*, and fig. 2 *B*), the tumor again assumed the shape, size and consistency of the portion at the cephalic level.

Microscopic Observations.—Microscopic study was made of each level of the spinal cord in paraffin and pyroxylin sections stained with hemalum and eosin, toluidine blue and Mallory's phosphotungstic acid-hematoxylin and by the methods of Van Gieson, Alzheimer and Mann, Bielschowsky and Weigert and Pal. Frozen sections were stained with sudan III.

At its uppermost level (fig. 2 *A*) the tumor was restricted to the central portion of the spinal cord. Its inner portion was cystic and contained a solid cord of hyalinized material, which on one side was firmly attached to the tumor tissue.

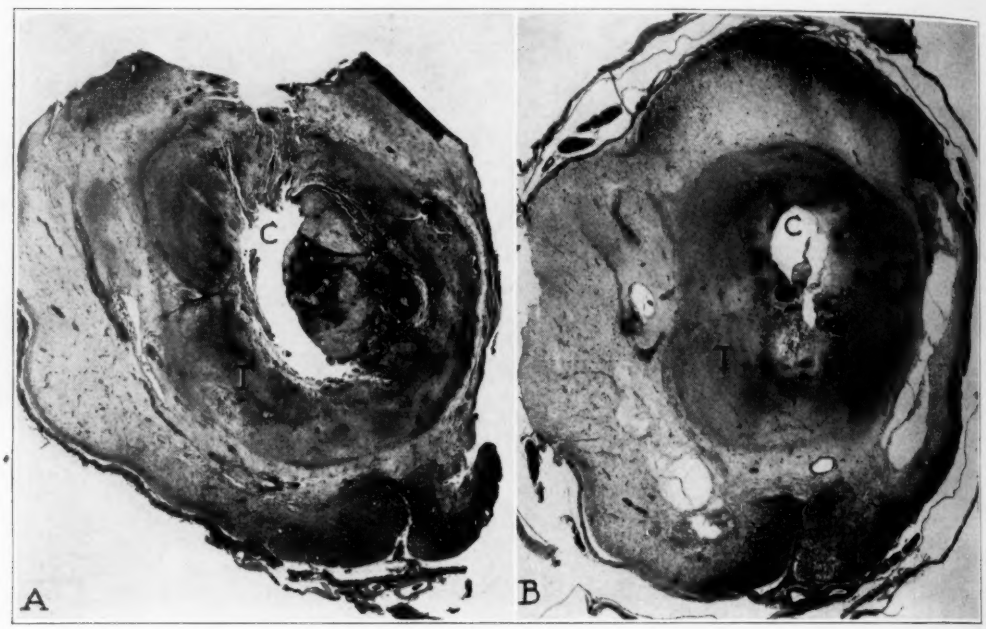

Fig. 2.—This picture shows segments *1* and *12* illustrated in figure 1 reproduced under higher magnification (Van Gieson stain; × 10). The similarity between the uppermost level *A* and the lowermost level *B* is evident. The intramedullary tumor (*T*) with the central cavity (*C*) is sharply demarcated from the surrounding parenchyma of the spinal cord.

This extended ventrally to the central canal, compressing and distorting the gray commissure, and invaded the gray substance, where it replaced entirely the lateral and posterior horns. In the white substance the tumor occupied the fasciculi laterales proprii, the most ventral portions of Goll's tract and the lateral columns, while the anterior columns and the subpial zone of Goll's columns appeared normal.

At the next level (fig. 3) the tumor was considerably larger. Ventrally, it extended to the anterior fissure and greatly compressed and distorted the anterior columns. Laterally, on the right side it extended to the pia mater, which here

was considerably thickened, and on the left it involved all but a narrow rim of the subpial white substance. The anterior columns were only rarefied and sievelike, but the remaining white substance was altered profoundly. At this level the central cavity was much larger and was eccentrically placed.

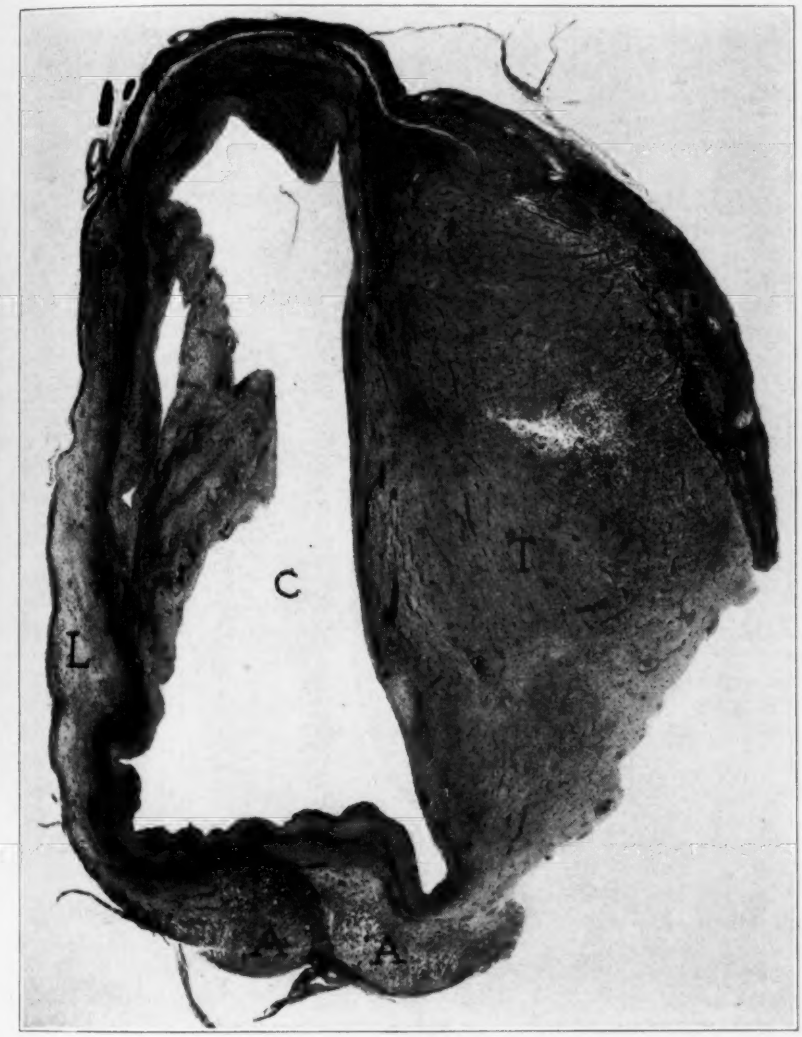

Fig. 3.—This picture shows segment *4* illustrated in figure 1 reproduced under higher magnification (Van Gieson stain; × 10). The tumor (*T*) consumes practically the entire section of the spinal cord except the anterior columns (*A*) and a subpial zone of white substance in the left lateral column (*L*). The cavity (*C*) is eccentrically placed, and the pia (*P*), where it is in direct contact with the tumor, is markedly hyperplastic.

At the next level (fig. 4) the spinal cord assumed the configuration of a hollow ovoid cylinder. The lining of the lumen consisted of a dense zone of tumor tissue, of varying thickness. Ventrally, the tumor extended to the anterior fissure and was everywhere separated from the pia by a zone of greatly altered white substance.

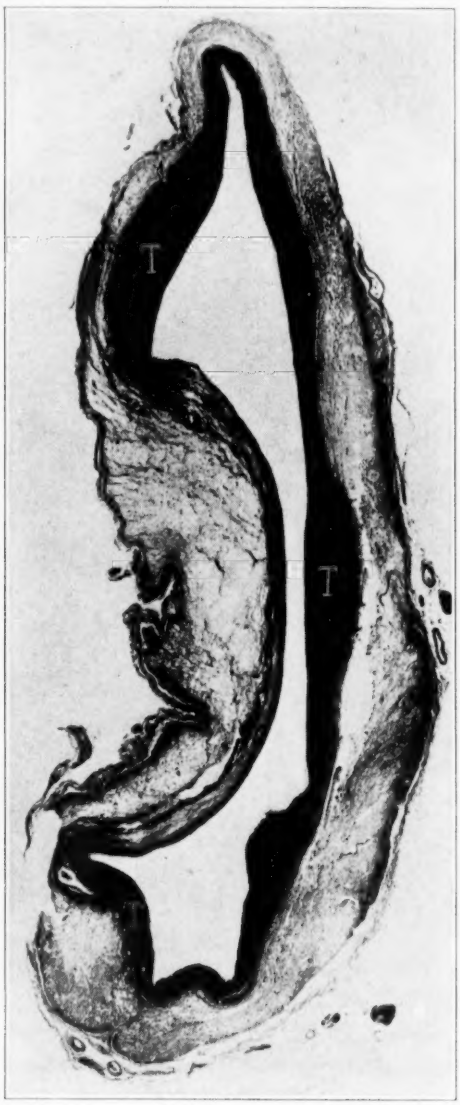

Fig. 4.—This section shows a higher magnification of segment 5 illustrated in figure 1 (Mallory's phosphotungstic acid-hematoxylin stain; × 10). The tumor (*T*) at this level is reduced to a narrow zone of varying width and harbors a much enlarged central cavity.

In the lowermost portions (fig. 2*B*) the spinal cord and the tumor assumed the configuration noted at the most cephalic level. Except for a small portion of the anterior columns and a narrow subpial zone in Goll's tract, the white substance of the lateral and posterior columns was severely altered.

The histologic structure of the tumor varied considerably, according to the level and the different portions of each level. The most striking changes were in the region where the tumor was grossly firm and gray-white (fig. 3). As it was here free from degenerative changes, its cellular and other structural components could be studied especially well. They were apparent even when examined with a low power lens, as the center of the tumor consisted of numerous ganglion cells. These were usually arranged in pairs or in small nestlike formations or were scattered singly among dense masses of glia nuclei and occasional microglia cells (fig. 5*A*). In addition there was in this region an abundance of thin-walled capillaries and larger blood vessels. With the silver method of Bielschowsky, the area revealed a loose meshwork of irregularly shaped nerve fibers, many of which could be traced directly to the ganglion cells (fig. 6*A*). The areas adjacent to the central cavity presented a different structure, consisting of parallel longitudinal rows of elongated and spindle-shaped glia nuclei, giving the field an appearance resembling that of a neurinoma (fig. 5*B*). The neurinoma-like areas contained large numbers of nerve fibers arranged in parallel rows (fig. 6*B*). Glia fibers and fibrils, with formations of isomorphous and anisomorphous gliosis, were present in both areas.

At the level represented in figures 2*A* and *B*, where the tumor was soft and light yellow-brown, ganglion cells were scarce or absent. Here the tumor consisted of a loose feltwork of glia fibrils in which were embedded large round or oval glia nuclei. Occasionally thin nerve fibers could be seen coursing through the gliogenous tissue.

Of similar structure was the tumor when transformed into a hollow cylinder. Nerve fibers were more abundant here than at the mentioned levels (fig. 2). They were long and straight and contained a delicate fibrillary structure. Capillaries and larger blood vessels with thickened adventitial walls were abundant. Embedded in the meshwork of glia fibrils, more especially in the portion adjacent to the syrinx, were immense numbers of macrophages, their cytoplasm filled with deep brown pigment material. An occasional ganglion cell was seen embedded in this dense glial stroma.

Ganglion Cells: Many of the ganglion cells were mature and fully developed. They were large and contained round or oval vesicular nuclei, with prominent nucleoli. The cytoplasm was rich in coarse granular Nissl bodies. Here and there an occasional ganglion cell containing two nuclei was seen (fig. 7). When stained with the method of Bielschowsky, the cytoplasm of the majority of the cells exhibited a fine feltwork of thin, argentophilic fibrils, which extended into the axon as well as into the dendrites. Whereas some of the ganglion cells were pear shaped, with a single, stout apical process (fig. 6*A*), other cells exhibited an abundance of dendrites, which sometimes were antler-like in appearance (fig. 8 *B*). Where the tumor was rarefied and contained recent extravasations of red cells, the ganglion cells were swollen, and their cytoplasm was homogeneous; they stained poorly and generally presented changes which Nissl described as acute cell disease. Except for a small number of coarse granular Nissl bodies about the nucleus and at the periphery of the cell, most of the Nissl substance was broken up and dustlike. When stained with silver, neurofibrils were observed to decrease in number, and many cells were devoid of processes. Some cells appeared vacuolated, their neurofibrils and Nissl bodies being displaced to the periphery.

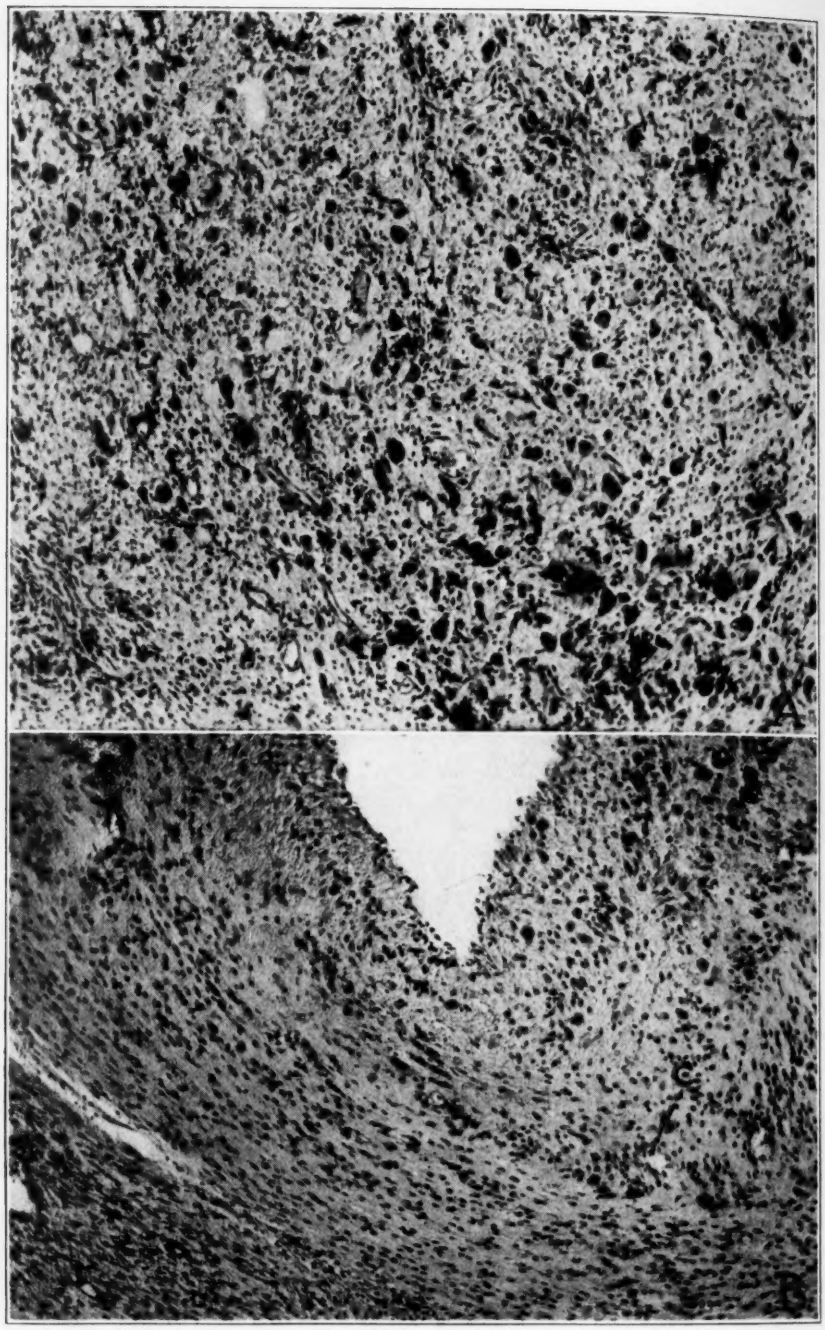

Fig. 5.—Sections (toluidine blue stain; $\times 100$) of the tumor (T) illustrated in figure 3. In A are a large number of ganglion cells, among which are scattered intimately a much larger number of glia nuclei. (B) Low power photomicrograph of the tumor (T) illustrated in figure 3, in the region adjacent to the central cavity (C). The neurinoma-like arrangement of the glia nuclei is evident. c indicates blood capillaries.

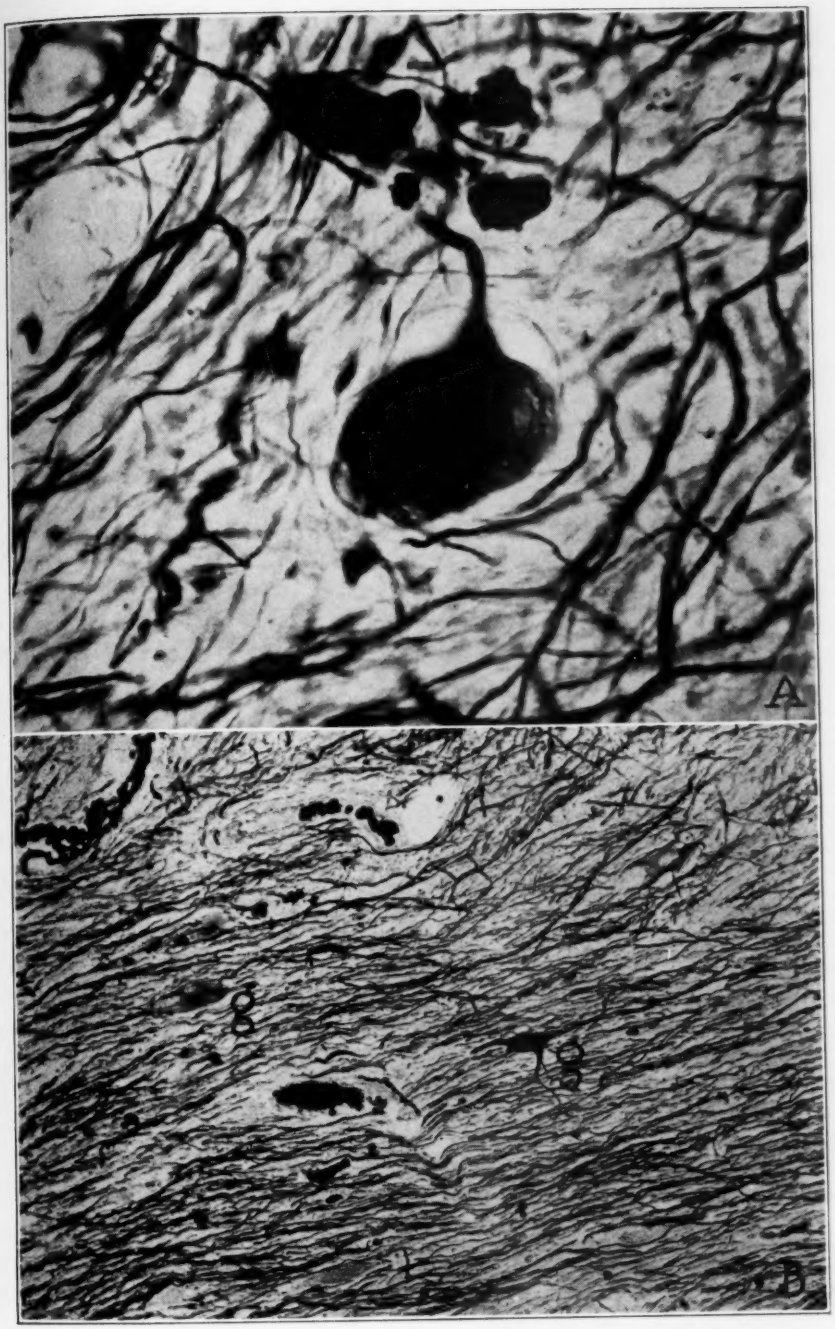

Fig. 6.—(*A*) High power photomicrograph (Bielschowsky stain; × 950) of the central portion of the tumor (*T*) shown in figure 3. The large, pear-shaped ganglion cell with a single stout process is embedded in a dense feltwork of nerve fibers of varying widths. (*B*) Lower power photomicrograph (Bielschowsky stain; × 200) of the neurinoma-like area seen in figure 5 *B*. The parallel bands of nerve fibers and the occasional ganglion cells (*g*) are reproduced under higher magnification in figure 8.

In the areas where the tumor was most severely degenerated, the ganglion cells were small, round and often fragmented. The nuclei were pyknotic. The cytoplasm stained homogeneously and was devoid of both Nissl bodies and neurofibrils.

Nerve Fibers: The number of nerve fibers in any visual field was far in excess of that of the ganglion cells. The fibers varied considerably in thickness, appearing as stout processes of ganglion cells or as fine fibrils that made up

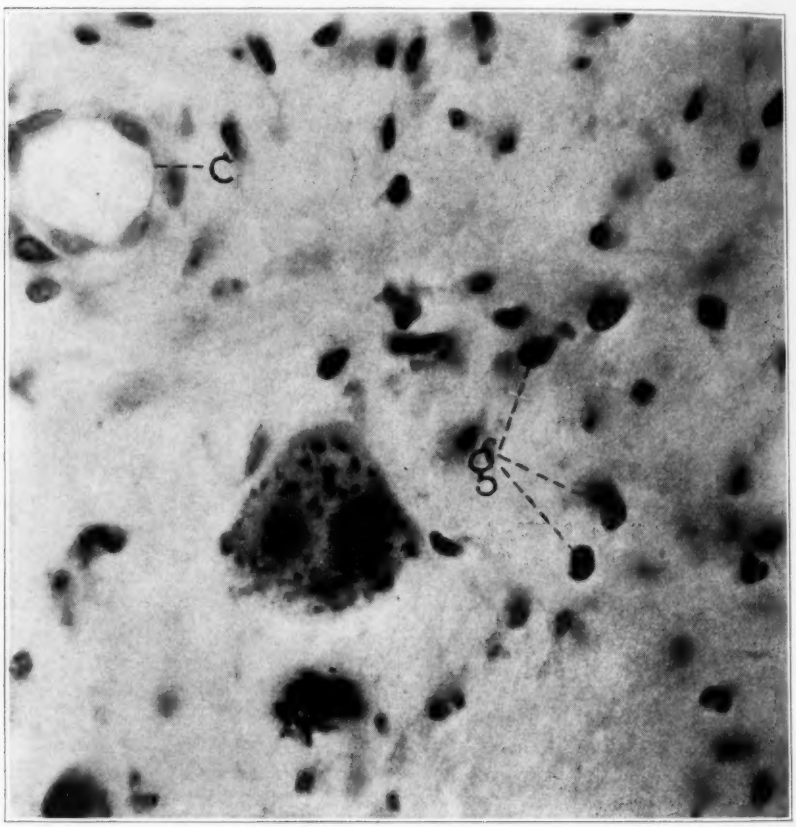

Fig. 7.—High power photomicrograph (toluidine blue stain; × 900) showing a binucleate ganglion cell with coarse Nissl bodies. *g* indicates glia nuclei, and *c*, a capillary.

the basic feltwork. All exhibited a fine neurofibrillar structure. The finer fibrils were often short, exhibited knoblike thickenings along their course and occasionally ended in bulblike formations. Many of the nerve fibers showed branching of the processes, but none exhibited anything resembling myelin sheaths.

Glia: Where the tumor was rich in ganglion cells, the glia nuclei exhibited no definite pattern. Generally they were round or oval and rich in chromatin granules. When stained with Mallory's method they showed, in addition to a narrow rim of pale-staining cytoplasm, numerous thin, steel-blue fibrils, which

emanated in every direction between the nerve fibers. In the neurinoma-like areas they appeared elongated and spindle shaped. At the levels where ganglion cells were absent, the glia nuclei were larger and vesicular, with a more generous rim of pale cytoplasm from which emanated many steel-blue fibrils.

Blood Vessels: In the areas rich in ganglion cells there was an abundance of thin-walled capillaries and large blood vessels with swollen endothelial cells.

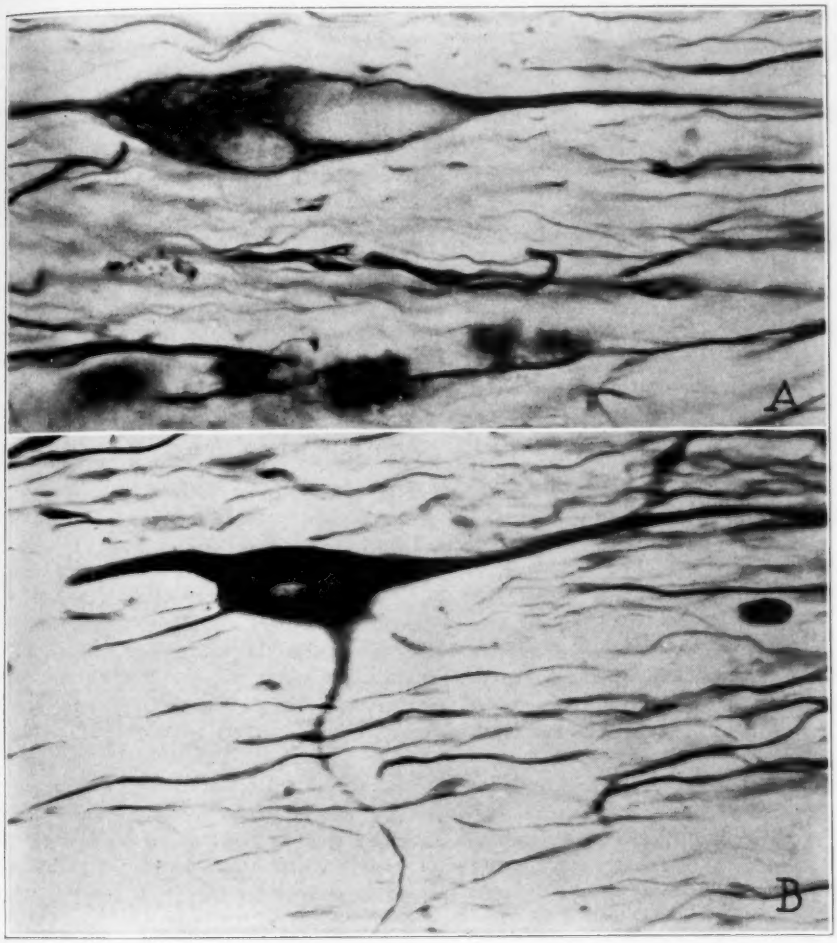

Fig. 8.—High power photomicrograph of the ganglion cells (*g*) in figure 6*B* (Bielschowsky stain; ×900). The cell in *A* is bipolar and contains a large vacuole, and that in *B* is multipolar, with an antler-like dendrite.

In other regions, for example, in the walls of the syrinx, as well as in the neurinoma-like areas, there was an abundance of thick-walled blood vessels which coursed longitudinally, parallel to the bundles of nerve fibers. The media of these medium-sized blood vessels was hyalinized and the adventitia markedly thickened. In most places the connective tissue fibers were restricted to the vicinity of the

blood vessels and did not extend into the substance of the tumor. Some of the adventitial spaces of the blood vessels were distended and filled with lymphocytes and plasma cells. These cellular infiltrations were most marked in the degenerated portions of the tumor, where the Virchow-Robin spaces were packed with hematogenous elements and large histiocytes, laden with golden-brown granules of blood pigment.

Degenerative Changes: In addition to the changes noted in the ganglion cells and the glia and nerve fibers, the tumor as a whole contained multiple foci of secondary degenerative changes, which could be traced definitely from the earliest stages to the final formation of a cavity. In some areas the fibrillary glial stroma was loosened and contained recent extravasations of blood. At the most cephalic level (fig. 2*A*) there was evidence of older and much larger confluent hemorrhagic areas, in the form of a solid, partially hyalinized node. This node contained calcium concretions and irregularly scattered islands of extravasated red cells, large numbers of mononuclear cells filled with blood pigment, polymorphonuclear leukocytes and occasional lymphocytes. The tumor tissue about this central mass was loosened. It contained numerous blood vessels with the media hyalinized, the adventitia thickened and the perivascular spaces filled with phagocytes packed with pigment. The aforementioned degenerative changes were present at all levels and were especially marked in the area in which the tumor tissue was reduced to a narrow rim (fig. 4). The meshes between the glia fibrils on the innermost layer of the syrinx were filled with histiocytes laden with blood pigment. In some areas connective tissue prolongations of the adventitia of the blood vessels extended into the glial tissue, parts of which it enveloped completely. In addition, calcium concretions of varying size were scattered here and there.

Changes Outside the Tumor: The tumor tissue was everywhere well demarcated from the adjacent parenchyma of the spinal cord by a zone rich in monster glia cells. These cells had round or oval nuclei, rich in chromatin, and a number of large cytoplasmic processes emanating from the perinuclear zone of the pale-staining cytoplasm. The processes of these cells intertwined with the glia fibrils of the tumor, on the one hand, and with the fibrils of the reactive gliosis of the white matter, on the other. The changes in the white matter were all secondary and need no detailed description. The nerve fibers exhibited various stages of secondary degeneration, with reactive glial phenomena—from the formation of myeloclasts and myelophages to that of various types of fat granule bodies.

Changes in the Meninges: The dura mater and the pia-arachnoid were thickened, especially over the nerve roots. The pia was particularly hyperplastic where it came into direct contact with the tumor. Here the proliferation of all layers was clearly evidenced by the presence of large numbers of elongated chromophore cells packed with pigment material in the innermost layers of the pia. These chromophore cells penetrated the ganglionic portion of the tumor for a short distance, forming pigmented bands. The external layer of the pia in this region was rich in collagen fibers, which stained bright red with the Van Gieson method.

COMMENT

Pathologic Aspects.—From the histologic description it is evident that the tumor consisted of large numbers of ganglion cells and nerve fibers embedded in a glial stroma. For this reason the tumor has been termed gangliogliomeuroma. Since the nerve fibers were nonmedullated, a more

proper designation would be ganglioglioneuroma amyelinicum. The ganglion cells and nerve fibers formed the most prominent part of the tumor. As in the cases of Foerster [1] and Pick and Bielschowsky,[2] binucleate ganglion cells were present. Some of the cells were fully developed and contained both Nissl bodies and neurofibrils, as well as dendrites and an axon. Regressive changes of ganglion cells, in the form of acute swelling, chromatolysis, disappearance of neurofibrils and tumefaction of both the cell body and its processes, were frequent. The disproportion between the number of nerve fibers and that of ganglion cells was striking, as has been reported previously in connection with this type of tumor. The glia was blastomatous in nature, and its fibril-forming properties were outstanding. Its neurinoma-like arrangement presented a picture similar to that in ganglioneuroma of the peripheral nervous system. The presence of cystic degeneration, as well as calcium deposits, has been described already (Bielschowsky).[5] Though, as has been emphasized, we concede the origin of the tumor to be from misplaced, undifferentiated cells of the lining of the primitive neural tube, the intramedullary mass constituted a true tumor and was not a heterotopy. For this reason, the neoplasm may be designated a hamartoma in the sense in which the term was used by Albrecht [6] to signify tumor formation from misplaced embryonic cells.

Of great pathologic interest was the area of the spinal cord which, on gross and superficial microscopic examination, resembled syringomyelia. At the outset, we wish to state that we use the term syringomyelia as a definite pathologic entity representing the pathologic features described by Petrén [7] and by Hassin.[8] According to Hassin, it is primarily a degenerative glial process, which may be termed abiotrophy of the glial tissue. With the degeneration of the glia, areas of homogenization develop and later break down, forming cavities. The cavities become lined with connective tissue derived either from prolongations of the pia or from the adventitia of the blood vessels. This picture is in sharp contrast to the conditions present in our case. No areas of homogenization were present, and the cavity was lined with blastomatous tissue in which there was a marked tendency to the formation of glia fibrils. The only similarity to syringomyelia in our case was the presence of a

5. Bielschowsky, Max: Das multiple Ganglioneurom des Gehirns und seine Entstehung, J. f. Psychol. u. Neurol. **32**:1, 1925.

6. Albrecht, Eugen: Die Grundprobleme der Geschwulstlehre, Frankfurt. Ztschr. f. Path. **1**:221, 1907.

7. Petrén, Carl: Beiträge zur pathologischen Anatomie und zur Pathogenese der Syringomyelia und der Syringobulbie, Virchows Arch. f. path. Anat. **196**: 377, 1909.

8. Hassin, George B.: A Contribution to the Histopathology and Histogenesis of Syringomyelia, Arch. Neurol. & Psychiat. **3**:130 (Feb.) 1920.

cavity. It is unfortunate that there is a tendency to classify a cavity in the spinal cord as syringomyelia, whether it is a focus of softening, a dilated central canal, a hemorrhage or a broken-down tumor. The aforementioned pathologic conditions do not give the well known and typical clinical picture of syringomyelia, nor do they represent the histologic changes seen in true syringomyelia. In our case, for instance, the genesis of the cavity could be followed step by step, from the earliest rarefaction of the tumor tissue and its destruction by a hemorrhage to the development of a picture superficially resembling syringomyelia. With Hassin,[9] we designate such cavities, including that in our case, pseudosyringomyelia, a term introduced by Phillippe and Oberthür [10] to differentiate it from true syringomyelia.

SUMMARY

1. A case of ganglioglioneuroma of the spinal cord is described.

2. Like many other types of intramedullary tumor, it possessed a cavity which resembled that of syringomyelia on superficial examination but did not on microscopic study.

3. A cavity occurring in or associated with an intramedullary tumor is not syringomyelia but pseudosyringomyelia, as demonstrated by the studies in the case recorded here.

9. Hassin, George B.: Histopathology of the Peripheral and Central Nervous System, Baltimore, Williams & Wilkins Company, 1933.

10. Phillippe, C., and Oberthür, J.: Contributions à l'étude de la syringomyélie et des autres affections cantaires de la moëlle épinière, Arch. de méd. expér. et d'anat. path. **12**:513, 1900.

Case Reports

MARIE'S ATAXIA (OLIVOPONTOCEREBELLAR ATROPHY)

Clinical and Pathologic Considerations

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In reporting a sporadic case of Marie's ataxia, which, as has been emphasized,[1] is the same morbid condition described by Dejerine and Thomas as olivopontocerebellar atrophy, I shall endeavor briefly to contrast the histologic changes in this case with those present in its hereditary form and in the sclerosed and the crossed type of cerebellar atrophy. Since Marie's ataxia is rarer than Friedreich's form, it is usually not recognized and is diagnosed instead as some other degenerative disease process—such as multiple sclerosis. A good instance of such an occurrence is presented by the case recorded here.

REPORT OF A CASE

History.—A man aged 52, white, was admitted to the Research Hospital on July 15, 1935, because of dizziness, tinnitus, unsteadiness of gait and disturbances of speech—of about three years' duration. During that period he had lost about 40 pounds (18.1 Kg.). The disturbances of gait were evidently of much longer duration, as relatives and friends long before that called the patient's attention to his peculiar gait, which was "less certain and less peppy." The condition grew worse steadily, and the patient, a conductor, had to give up work three years before he was admitted to the Research Hospital. There was no history of venereal infection. The patient had had smallpox, influenza and a number of accidents (injury to the lower part of the back, a fall on the head and fracture of a rib). He also had undergone operations on the tonsils and sinuses.

The father had died at the age of 80 (probably of arteriosclerosis), and the mother died at the age of 76, of a "stroke." Two brothers (aged 54 and 56, respectively) and one sister (aged 50) were living and well. The wife had had no miscarriages or stillbirths.

Examination.—The patient was tall and poorly nourished, and yet cheerful. His speech was slow and somewhat scanning. The extremities, especially the left, exhibited motor weakness, ataxia and adiadokokinesis. The tendon reflexes were markedly increased throughout, with a Rossolimo sign bilaterally. All modes of

Read before the Chicago Neurological Society, Jan. 21, 1937.

From the Division of Neuropathology, the University of Illinois College of Medicine.

1. Hassin, George B., and Harris, Titus H.: Olivopontocerebellar Atrophy, Arch. Neurol. & Psychiat. **35**:43 (Jan.) 1936.

sensation, including the vibratory sense and the sense of position, were normal; there were urinary disturbances (retention), which progressed rapidly and caused the patient's death (on July 28) about two weeks after his entrance to the hospital.

Comment and Course.—Thus, the clinical picture was not rich in signs or symptoms. The outstanding features were disturbances of gait and speech, tinnitus, exaggerated tendon reflexes and marked urinary disturbances. While at the Research Hospital, the patient had been examined repeatedly by Dr. R. P. Mackay, and two years before by Dr. F. P. Moersch, at the Mayo Clinic. Three days after the patient's admission to the hospital Dr. Mackay noticed a slight rhythmic tremor in the right thumb, a masklike facies, mild nystagmus (to the right and left and perhaps vertically) and monotonous speech, with some scanning and slurring. In addition he noted a cogwheel phenomenon in both arms, definite hypertonia in the legs, incoordination in the arms and normal reflexes, with no Babinski or Hoffmann sign. The abdominal reflexes were equal. "The rebound phenomenon was 2+, and there was little or no parkinsonian finger wiggle," while "adiadokokinesia was 2+ in both hands." Dr. Mackay interpreted the clinical picture as "chronic encephalitis with parkinsonism and involvement of the brain stem and the vestibular mechanism, as evidenced by the nystagmus." As to the signs of cerebellar involvement, Dr. Mackay stated merely that they are uncommon in encephalitis.

Some of the findings of Dr. Mackay were evidently not constant, for six days after the first examination the cogwheel phenomenon was mild, speech was "pseudobulbar and there were a 2+ sucking reflex and an automatic bladder." At this time Dr. Mackay considered also the possibility of a tumor of the brain.

Spinal puncture revealed 128 cells per cubic millimeter, a 2+ Pandy reaction and normal pressure. The blood pressure was 132 systolic and 80 diastolic, and the hemoglobin content was 70 per cent.

The urinary disturbances grew worse. Acute cystitis developed, which necessitated repeated catheterization, and was followed by pulmonary edema and death.

Dr. Moersch, who had examined the patient two years before, at the Mayo Clinic, summed up his findings in a letter, as follows: "There were marked horizontal and slight vertical nystagmus; marked incoordination of all extremities, with good motor power; exceedingly ataxic gait, with no signs of changes in the pyramidal tracts; slightly diminished abdominal reflexes; normal deep reflexes, and no Babinski sign." Though Moersch considered tumor of the brain, he had "the impression of cerebellar ataxia, on a degenerative basis."

The scanning speech, tremor (though not constant), ataxia and lively reflexes suggested multiple sclerosis, but such a diagnosis was not considered seriously, mainly because of the patient's age.

Necropsy.—No particular gross anomalies were noted in the brain and its coverings. Pyroxylin (celloidin) sections stained by the method of Pal and Kultschitzky revealed atrophy of the ventral portion of the pons (fig. 1), with preservation of the pyramidal fibers and the issuing fifth nerve on each side, atrophy of the brachia pontis (the middle cerebellar peduncles) and reduction in the size and number of the cores (white substance) of some lamellae of the cerebellum (fig. 2). With the aforementioned staining method no noteworthy changes were demonstrated in the medulla, where only the olivocerebellar fibers appeared to be reduced in number, or in the midbrain and the cerebral hemispheres; but extensive changes could be demonstrated with nuclear and silver staining methods. Thus, in the ventral part of the pons practically all the ganglion cells

were affected (fig. 3). Fairly well preserved ganglion cells were scarce, but even such cells appeared tumefied, and the Nissl bodies were lacking. The majority of the ganglion cells were broken up into fragments or were converted into a shapeless, poorly staining substance, which was scattered over the visual field among numerous astrocytes, oligodendrocytes and microglia and gitter cells (fig. 3). A great number of ganglion cells were homogeneous and of small size.

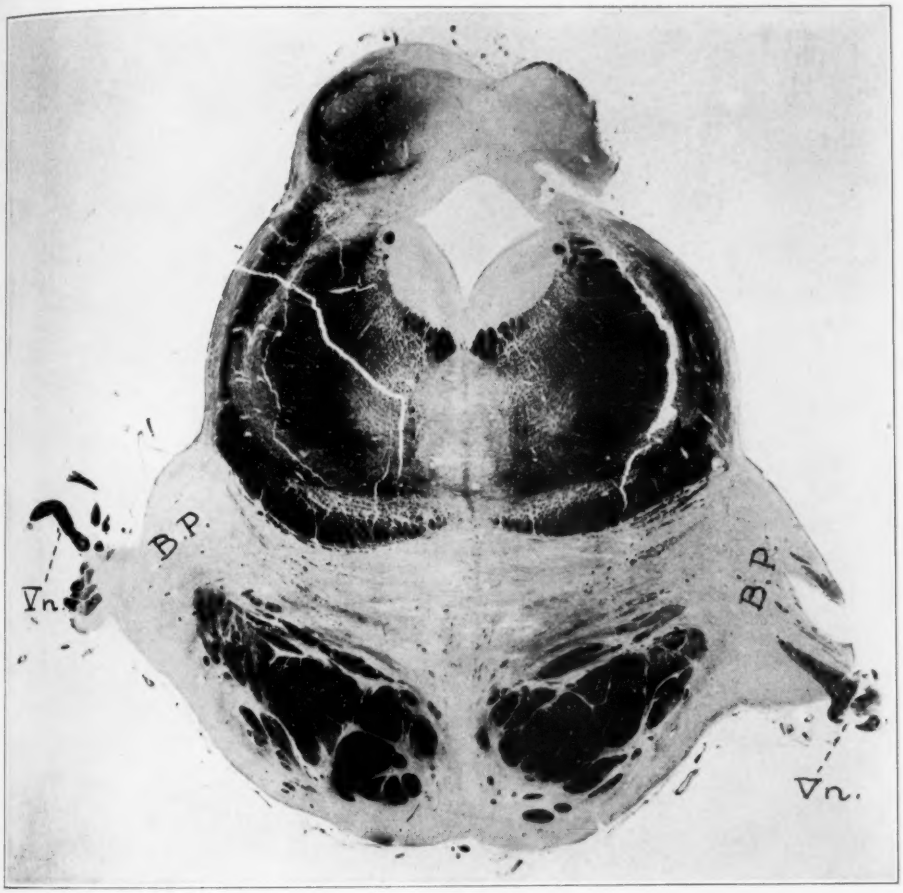

Fig. 1.—Cross-section of the pons (Pal-Kultschitzky stain). The basal portion exhibits atrophy of the transverse fibers and the brachia pontis (*B. P.*) and preservation of the fifth nerves (*Vn.*), the pyramidal bundles and the tegmentum. The pallor of the right quadrigeminal body is due to an inborn anomaly.

As they were devoid of processes, they appeared round. Other ganglion cells were pale and granular and were often replaced by neuronophages. The cell changes described undoubtedly were responsible for the atrophy of the transverse fibers of the pons and the pontile brachia, which consisted of fibrous and cytoplasmic astrocytes and were transformed into a glial tissue scar. There were also newly

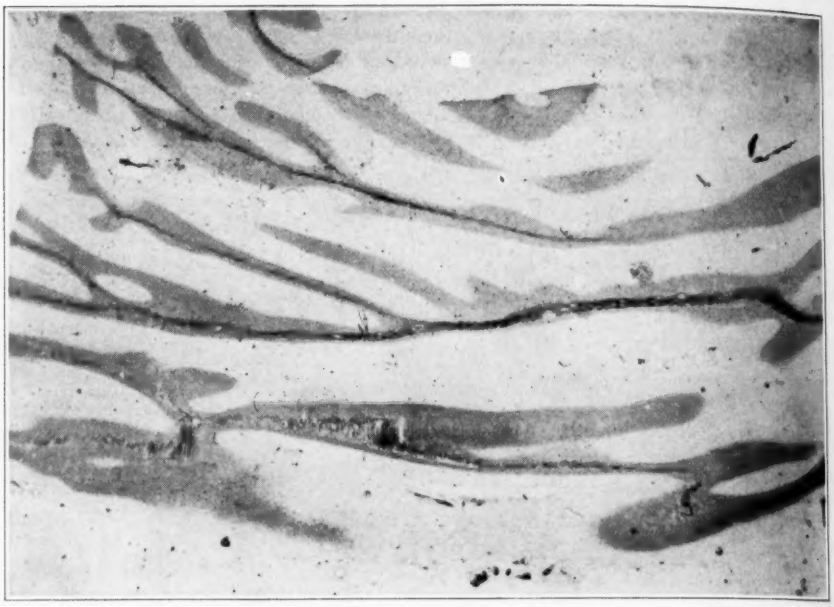

Fig. 2.—Section from the cerebellum (Weigert-Pal stain). The cores of the lamellae are thinned and poor in fibers. A photomicrograph of the cores, stained with toluidine blue, is shown in figure 5.

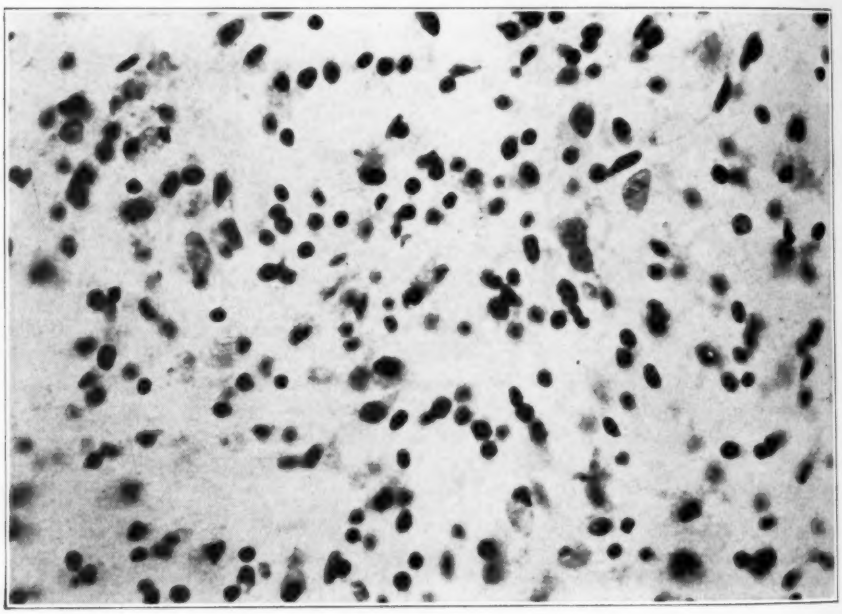

Fig. 3.—Cells of the pons, which are described in the text. Toluidine blue stain.

formed capillaries, but the blood vessels showed no changes except hyperplastic and thickened walls. Some processes of the astrocytes invaded the pyramidal bundles, where they enveloped individual nerve fibers, which, as noted, exhibited no structural changes.

Similar changes were noticed in the ganglion cells of the olives (fig. 4) of the medulla, especially in their most caudal portions. As in the pons, the cell bodies were reduced in size, they appeared as though shriveled, atrophied or sclerosed and always exhibited satellitosis and neuronophagia. Many ganglion cells harbored granules of pigment in their cytoplasm. In some instances these were numerous. Some ganglion cells were homogeneous or were broken up or replaced by glial tissue. The ganglion cells of the arcuate nuclei were practically normal,

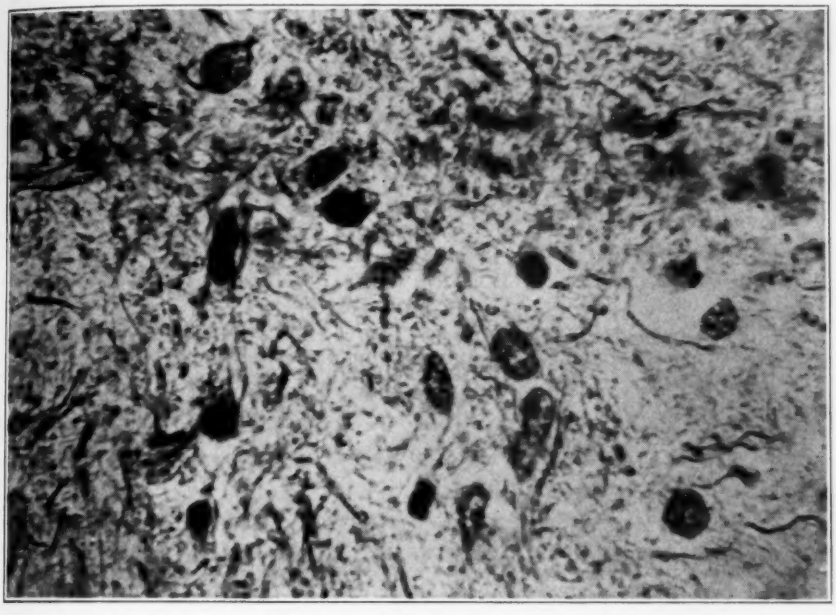

Fig. 4.—Microscopic appearance of the olives, a description of which appears in the text. Bielschowsky stain.

and the ventral arcuate fibers were normal accordingly. The olivocerebellar fibers, as stated, were rarefied, but no changes were observed with the silver staining method in the corpus restiforme, the stria acusticae, the raphe or the cranial nerves and their nuclei. Essick's corpus pontobulbare could not be demonstrated in this case.

Cerebellum: The paucity of the myelin fibers in the cores (white substance) of some cerebellar lamellae was combined with immense cellularity (fig. 5), demonstrable in sections stained with toluidine blue and similar methods. Under a higher power lens, the individual cells appeared round, oval or rod shaped and were rich in chromatin; some were kidney shaped and large and, like those just described, were mixed with gitter cells. With the silver staining method of Bielschowsky, it was possible to demonstrate that the majority of the cells were astrocytes and that there also were numerous newly formed capillaries. Neither

the granular or the molecular layer nor the Purkinje cells themselves exhibited noteworthy changes. Only in the upper vermis did the granular layer appear slightly rarefied and the adjacent white substance sclerosed.

Substantia Nigra: The substantia nigra contained the usual wealth of ganglion cells, which were packed with melanin (fig. 6). The form of the pigment cells was generally preserved; the size of some appeared slightly reduced, as if the cells were fragments. Associated glial reactive phenomena or the presence of

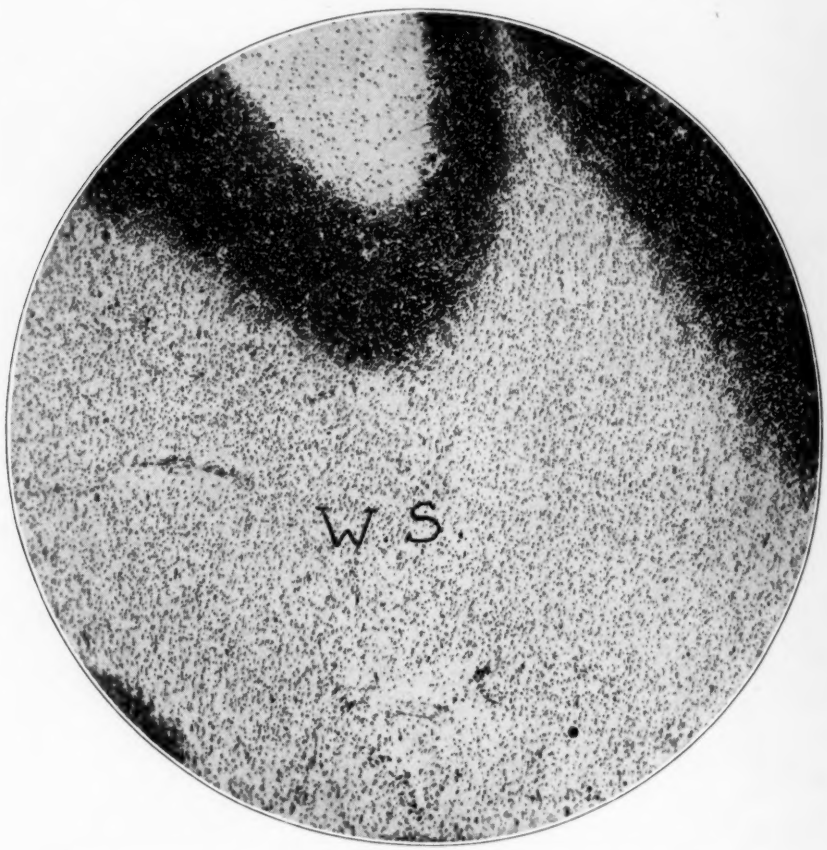

Fig. 5.—Section from the semilunar lobe of the cerebellum (toluidine blue stain), showing the presence of Purkinje cells. The white substance (*W.S.*) is exceedingly cellular.

pigment in the glia cells could not be demonstrated with the methods of Holzer and Alzheimer, and for this reason the anomalies mentioned should not be considered pathologic.

Nucleus Ruber: Here some ganglion cells were disrupted and disfigured and exhibited phenomena of neuronophagia. The majority of ganglion cells, however, were preserved and there were occasional cytoplasmic astrocytes and newly formed capillaries.

Basal Ganglia, Cerebral Cortex and Spinal Cord: Still scarcer were the changes in the basal ganglia, where the only anomaly was the presence of occasional newly formed capillaries. Nor were any changes demonstrable in the cortex or in the small stump of the spinal cord attached to the medulla.

Summary of Pathologic Observations.—There were atrophic, degenerative changes in the medullary olives, the basal portion of the pons and the white substance of some cerebellar lamellae—a picture of olivopontocerebellar atrophy.

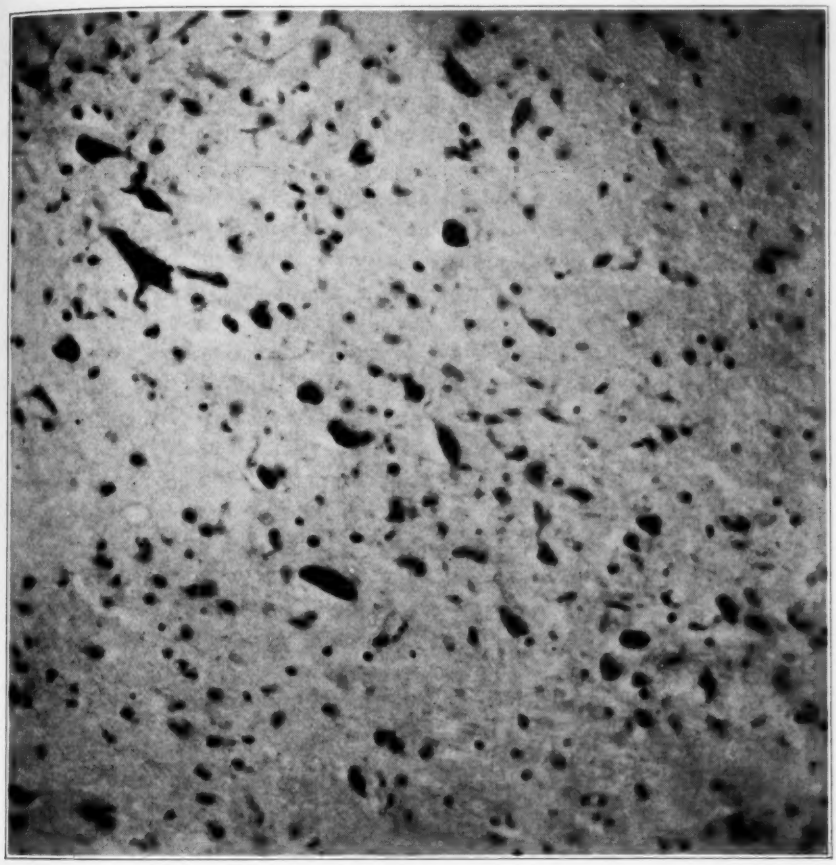

Fig. 6.—Zona impacta of the substantia nigra (toluidine blue stain). The black masses are ganglion cells filled with melanin.

COMMENT

The changes described were observed in a man who began in the sixth decade of life to experience ataxia, incoordination in both the upper and the lower extremities and disturbances of speech and gait—all of which were followed by pronounced urinary disturbances, which

were the cause of death. Urinary complications, emphasized by Bakker [2] in olivopontocerebellar atrophy, are frequently observed in this disease, though Bakker could not give a plausible explanation of their genesis. In the present case they appeared late and were probably accidental. The clinical picture on the whole suggested a variety of pathologic conditions, among them multiple sclerosis and some form of degenerative disease process of the cerebellum. The most common types of cerebellar degeneration are sclerotic atrophy [3] (classified by Marie, Foix and Alajouanine as late cerebellar, predominantly cortical [4]) and olivopontocerebellar atrophy. Clinical differentiation between cerebellar atrophy and multiple sclerosis is not always possible and is usually more or less conjectural. The differential points given by Marie and his co-workers [4] are probably too dogmatic and artificial. According to them, multiple sclerosis (cerebellar type) is manifested by tremor, followed by asynergy and incoordination. In the type of cerebellar atrophy which they described as late,[4] the order of the signs is reversed: First, there is incoordination, followed by asynergy and tremor; the onset is late in life, and the incoordination is mainly in the lower extremities. In multiple sclerosis, on the other hand, the incoordination is prevalent in the upper extremities; the onset is early in life, and the disturbances of speech are more marked. In olivopontocerebellar atrophy, incoordination is present in both the upper and the lower extremities, and speech is much less affected. Artificial as the differential points given by Marie, Foix and Alajouanine are—for on the whole one must concede that the differences are quantitative—it is well to bear in mind their apt suggestion: that a cerebellar lesion should be suspected in a person older than 50 who shows no signs of intracranial hypertension and exhibits marked bilateral and symmetrical disturbances of coordination and equilibrium, especially in the lower extremities. Though the authors had in mind their type of cerebellar atrophy (late cortical [4]), their suggestion may also be applied safely to the olivopontocerebellar type as well. In cases of the hereditary or familial form of the latter, diagnosis is easier than in a sporadic case, for the onset is much earlier in life (in the second or the third decade), the duration of the disease is much longer and the clinical manifestations are more pronounced, because more advanced. The histologic changes, accordingly, are more marked, especially in the pons and medulla, while the cerebellum is always less

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3. Hassin, George B.: Sclerotic Atrophy of the Cerebellum: Report of Two Cases, Arch. Neurol. & Psychiat. **31**:1205 (June) 1934.

4. Marie, P.; Foix, C., and Alajouanine, T.: De l'atrophie cérébelleuse tardive à prédominance corticale (atrophie parenchymateuse primitive des lamelles du cervelet; atrophie paléocérébelleuse primitive), Rev. neurol. **38**:849 and 1082 (July) 1922.

affected in both the sporadic and the familial type. The changes in the cerebellum, as has been emphasized elsewhere,[1] are secondary to those in the pons and medulla and, as the present case shows, may spare the ganglion cells of the cerebellar cortex. Thus they may be confined to the white substance of some cerebellar lamellae. In sclerotic atrophy of the cerebellum[3] (also known, as noted, as the late form of Marie, Foix and Alajouanine[4]), the primary changes are in the ganglion cells (Purkinje cells, granular layer cells, etc.), that is, in the gray matter of the cerebellum, and the degeneration involves their axons or the efferent fibers of the white substance. In olivopontocerebellar atrophy the degeneration involves the afferent fibers of the nerve substance, and as the atrophy is long standing and its onset early, it may cause retrograde or transsynaptic degeneration of the cerebellar cortex. The same may be said of crossed atrophy of the cerebellum (this has been discussed elsewhere[5]). However, a clinical diagnosis of crossed atrophy of the cerebellum cannot be suspected, since the clinical picture is dominated by manifestations of cerebral involvement. For this reason, the only types of atrophy of the cerebellum that may exhibit a suggestive clinical picture are the sclerotic[3] (Marie's late cortical form[4]) and the olivopontocerebellar. Though Marie, Foix and Alajouanine observed in the sclerotic type some involvement of the olives, the histologic changes, in general, are so different in the two types that they should be considered as distinct morbid entities. As has been shown,[1] they represent degeneration of certain systems of ganglion cells—of the various layers of the cerebellar cortex, in one form, and of the systems of ganglion cells of the olives, pons and arcuate nuclei (the cell bands of Essick), in the other. With amyotrophic lateral sclerosis or its components (progressive muscular atrophy of the Aran-Duchenne type, progressive bulbar paralysis and, probably, Mills' disease —primary degeneration of the motor cortical cells), the two forms of cerebellar atrophy under discussion form one vast group of nuclear atrophies. They are all manifestations of what C. and O. Vogt called *Pathoklyse*—abnormal vulnerability of certain groups of cells or fibers. Scherer[6] and others expressed the belief that the white substance is affected primarily and that changes in the ganglion cells are secondary. If such is the case, one must assume that the pathologic process is similar to that seen in subacute combined degeneration of the cord, Friedreich's ataxia, Schilder's disease, multiple sclerosis and some other conditions in which the degenerative process in the nerve fibers may last

5. Hassin, George B.: Crossed Atrophy of the Cerebellum: Pathologic Study of a Case, Arch. Neurol. & Psychiat. **33**:917 (May) 1935.

6. Scherer, Hans-Joachim: Beiträge zur pathologischen Anatomie des Kleinhirns: Genuine Kleinhirnatrophien, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:335, 1933.

for years without causing evident secondary changes in the ganglion cells. Axonal reaction of the ganglion cells following destruction of the axons may, under certain conditions, result in their atrophy. Such an explanation may be given for the atrophy of the cortical ganglion cells of the cerebellum in the hereditary form of olivopontocerebellar atrophy and in the crossed atrophy of the cerebellum in which the duration is exceedingly long—practically throughout life. But in sporadic cases of olivopontocerebellar atrophy, such as are recorded in this paper, in which the duration of the disease process is much shorter, the ganglion cells of the cerebellar cortex may remain unaffected or be changed only slightly. For instance, in the present case no changes in the cortex of the cerebellum were demonstrable, yet marked degeneration was present in the white substance, which, as has been stated, was secondary to the degenerative conditions in the pons and the medulla. Nor were changes observed in the nucleus ruber, the substantia nigra, the basal ganglia and the cerebral cortex. In short, I could see no changes in the extrapyramidal system which have been emphasized by Scherer [6] in his cases of olivopontocerebellar atrophy. Nor could I observe them to be pronounced in the cases of Keiller [7] which I studied, though the specimens at my disposal did not lend themselves to proper study. They were too old; the sections had been stained mostly with the Weigert-Pal method and, in general, were not convincing. At any rate, if there were changes in the substantia nigra and the nucleus ruber, they were by no means as striking as they are in parkinsonian states.[8] When compared with those in the pons or the medulla, they appeared altogether insignificant.

CONCLUSIONS

1. Olivopontocerebellar atrophy may occur as a sporadic or as a hereditary familial disease. It is distinct from a more common type of cerebellar atrophy, known as sclerotic, or late cortical cerebellar atrophy, and under other names.

2. The histologic changes of olivopontocerebellar atrophy vary, depending on the duration of the disease process, and are generally much more pronounced in the hereditary-familial than in the sporadic type.

3. The clinical picture is not characteristic. It may resemble not only a cerebellar lesion but a disseminated cerebrospinal disease, such as multiple sclerosis.

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7. Keiller, W.: Four Cases of Olivo-Ponto-Cerebellar Atrophy Giving a History of Heredity with Three Autopsies, South. M. J. **19**:518 (July) 1926.

8. Hassin, George B., and Bassoe, P.: Parkinsonian States: Clinico-Pathologic Studies, Arch. Neurol. & Psychiat. **15**:218 (Feb.) 1926.

4. The olivopontocerebellar and sclerotic types of atrophy of the cerebellum are the main, if not the only, types to be considered and differentiated from other obscure clinical forms, which are hard to classify and define.

DISCUSSION

DR. R. P. MACKAY: In order that the neurologist may capitalize on the contributions of the pathologist, it is necessary to pay especial attention to the clinical features in such cases as this. I was fortunate in being able to make a clinical study of the patient whose case Dr. Hassin has so well described pathologically. When I first saw him, he was lying in bed in a rigid posture, with masked facies. Examination also revealed rhythmic tremor and a cogwheel phenomenon in the arms, so that the suggestion of parkinsonism was strong. Further examination, however, revealed nystagmus, scanning and ataxic speech, definite adiadokokinesis and a degree of ataxia which practically prevented him from walking. This syndrome of parkinsonism with cerebellar dysfunction was new in my experience, and chronic encephalitis was considered the probable diagnosis, although I had never seen it produce such a clinical picture. The pathologic study, revealing olivopontocerebellar atrophy, greatly surprised me.

Thus, the clinical differentiation between this disease and chronic encephalitis may be difficult. The presence of extrapyramidal disturbances in olivopontocerebellar atrophy has been emphasized by several observers in France and Germany (Guillain, G.; Mathieu, P., and Bertrand, I.: Étude anatomoclinique sur deux cas d'atrophie olivo-ponto-cérébelleuse avec rigidité, *Ann. de méd.* **20**:417 [Nov.] 1926, Scherer, H. J.: Extrapyramidale Störungen bei der olivopontocerebellaren Atrophie: Ein Beitrag zum Problem des lokalen vorzeitigen Alterns, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **145**:406, 1933). It is probable that rigidity of the parkinsonian type, with rhythmic tremors or athetoid movements, must be considered as often constituting a part of the clinical picture of the disease, associated, of course, with signs of cerebellar dysfunction.

Dr. Hassin also mentioned that the differential diagnosis between this disorder and multiple sclerosis may be difficult. Dr. Hall and I have discussed this problem (Hall, G. W., and Mackay, R. P.: Forms of Familial Ataxia Resembling Multiple Sclerosis: A Clinical Study, ARCH. NEUROL. & PSYCHIAT. **37**:19 [Jan.] 1937). Patients with olivopontocerebellar atrophy often have nystagmus, scanning speech and intention tremor—signs which constitute Charcot's triad. Certain features, however, enable one to separate cases of this disease from the group of multiple sclerosis. Although the onset is usually in early adult life, as in multiple sclerosis, the course of the disease is progressive and not remittent. Furthermore, there are no signs of disturbance of the pyramidal tract in patients with olivopontocerebellar atrophy and no evidence of involvement of the dorsal columns, such as loss of vibration sense. Finally, in many cases a history of familial incidence will be obtained, which speaks strongly against multiple sclerosis.

I believe that olivopontocerebellar atrophy is more common than is realized and that in many cases the condition at present is diagnosed as multiple sclerosis.

DR. GEORGE W. HALL: I am interested in Dr. Hassin's paper, as he knows so much about the pathologic picture in this condition. I think he should have made the clinical diagnosis. The three so-called cardinal symptoms of multiple sclerosis can no longer be relied on for a diagnosis of this disease, i. e., nystagmus, scanning speech and loss of abdominal reflexes. In one of the cases of this disease in the series reported by Dr. Mackay and me, I had previously made a diagnosis of multiple sclerosis. The same diagnosis had been made at two reliable hospitals. The patient then returned to our office, and at that time we were able to obtain a definite family history for the first time, which enabled us to eliminate multiple sclerosis. While patients with this disease have Parkinson's syndrome, intention tremor, nystagmus and scanning speech, I think the absence of the Babinski sign and the presence of the abdominal reflexes should put one on guard in arriving at the proper diagnosis.

DR. MABEL G. MASTEN: Is there such a condition as cerebellitis?

DR. G. B. HASSIN: Instead of cerebellitis, the term cerebellar encephalitis is used by some, and Oppenheim, in his textbook, speaks of the cerebellar localization of encephalitis.

I cannot add much to what Dr. Mackay, Dr. Hall and I have emphasized. The purpose of my demonstration of a sporadic case of olivopontocerebellar atrophy, or Marie's atrophy, was to call the attention of my friends (and "non-friends") to a morbid condition which may resemble multiple sclerosis and present great diagnostic difficulties. Especially difficult is it, as pointed out by Marie and his co-workers, to differentiate this disease from certain cerebellar degenerative processes, which should always be borne in mind before a diagnosis of multiple sclerosis is made.

Technical and Occasional Notes

VIBRATION SENSE

LEWIS J. POLLOCK, M.D., CHICAGO

Within recent years controversies have arisen as to the nature of the vibration sense. At first, chiefly as the result of clinical observation, it was thought that the receptors for vibration sense were present in the muscles, tendons, periosteum and bones and perhaps the arteries and that sensations traveled from them with other forms of proprioceptive sense.

As early as 1889, Rumpf [1] concluded that the receptors were limited to the skin. In the school of investigators who believe that the receptors for vibration sense are limited to the skin, differences of opinion exist as to whether they are of the character of pressure receptors, as held by von Frey,[2] or are associated with an independent aspect of touch, as supported by Katz.[3] Some differences of opinion are due to lack of clearness in terminology; for example, the interpretation of deep sensibility as subcutaneous sensibility instead of a physiologic division which may be evoked either in the skin or in the subcutaneous tissues.

Some conclusions are the result of philosophic argument, as illustrated by a statement of Katz [1] that if the elbow is pressed against a sounding box which supports a large vibrating tuning fork a sensation of vibration will be felt in the hand, even though it is not in contact with the vibrating body and there is no specific pressure sensation.

Other conclusions result from a comparison of the fatigability of touch and vibratory sense (Katz, Kampie [4]), differences in adaptation of pressure and tactile mechanisms, those for pressure proceeding less rapidly (Adrian [5]), and differences in the reaction times of vibratory and pressure sense (Fessard [6]). Finally, conclusions have been reached as the result of clinical research in which in certain conditions touch,

Read at a meeting of the Chicago Neurological Society, Feb. 20, 1936.

From the Department of Nervous and Mental Diseases, the Northwestern University Medical School.

1. Rumpf: Ueber einen Fall von Syringomyelie nebst Beiträgen zur Untersuchung der Sensibilität, Neurol. Centralbl. **8**:185, 1889.

2. von Frey, M.: Die Vergleichung von Gewichten mit Hilfe des Kraftsinns, Ztschr. f. Biol. **65**:203, 1915.

3. Katz, D.: The Vibratory Sense and Other Lectures, Maine Bull. **32**:10, 1930.

4. Kampie, A.: Experimentelle Untersuchungen über die praktische Leistungsfähigkeit der Vibrationsempfindungen, Arch. f. d. ges. Psychol. **76**:3, 1930.

5. Adrian, E. C.: The Basis of Sensation, New York, W. W. Norton & Company, Inc., 1928.

6. Fessard, A.: Du minimum d'énergie nécessaire pour l'excitation tactile, Compt. rend. Soc. de biol. **105**:699, 1930.

usually crudely examined, was found to be preserved whereas vibration sense was absent. Whether tactile sensibility is also affected, as could be determined only by more accurate examinations, remains to be determined.

Recently, numerous devices have been designed to test the sensibility of the skin to mechanical vibration. Most of these have been oscillator-driven vibrators. Tilney,[7] in a study of Helen Keller and Laura Bridgman, used a special pallesthesiometer recording on a scale of radio cycles, with a specially devised loud-speaker mechanism for the vibrator. Excellent oscillators and vibrators have been described by Knudsen[8] and especially by Gilmer.[9] These studies have been concerned chiefly with such subjects as the lower and upper frequency limits to which the sense of touch responds and the sensibility of touch as a function of frequency and of small differences of amplitude.

Whether the receptors for vibration sense reside in the cutaneous or the subcutaneous tissues or both, if one could examine an area devoid of epicritic and protopathic sensibilities a crucial test could be made as to whether any vibration sense is mediated by deep sensibility in a physiologic sense. This is the condition when the sensory root of the fifth cranial nerve is severed. Except for the border, the entire area of the cutaneous sensory supply of the fifth cranial nerve shows loss of epicritic and protopathic sensibility.

The preservation of some forms of deep sensibility, for example, pressure pain, after section of the sensory root of the fifth cranial nerve has been demonstrated by Davis[10] and by Ivy and Johnson.[11]

Maloney and Kennedy[12] examined patients with sections of various parts of the fifth cranial nerve and stated that when examined with a tuning fork the patient usually was unable to perceive vibration over the anesthetic side; rarely was there complete loss of vibration sense in the tongue. In all cases in which vibration was preserved on the affected side it was described as weaker than or different from that produced by the same stimulus on the sound side.

METHODS AND RESULTS OF INVESTIGATION

The apparatus used in this study consisted of a vacuum tube oscillator with a Hartley circuit and a three stage radio amplification. The vibrator consisted of reed driven by a phonograph pick-up, the reed vibrating as an extension of its armature. Frequencies of from 1 to 1,400 cycles per second were used. The

7. Tilney, Frederick: A Comparative Sensory Analysis of Helen Keller and Laura Bridgman: I. Mechanisms Underlying the Sensorium, Arch. Neurol. & Psychiat. **21**:1227 (June) 1929.

8. Knudsen, V. O.: "Hearing" with the Sense of Touch, J. Gen. Psychol. **1**:320 and 352, 1928.

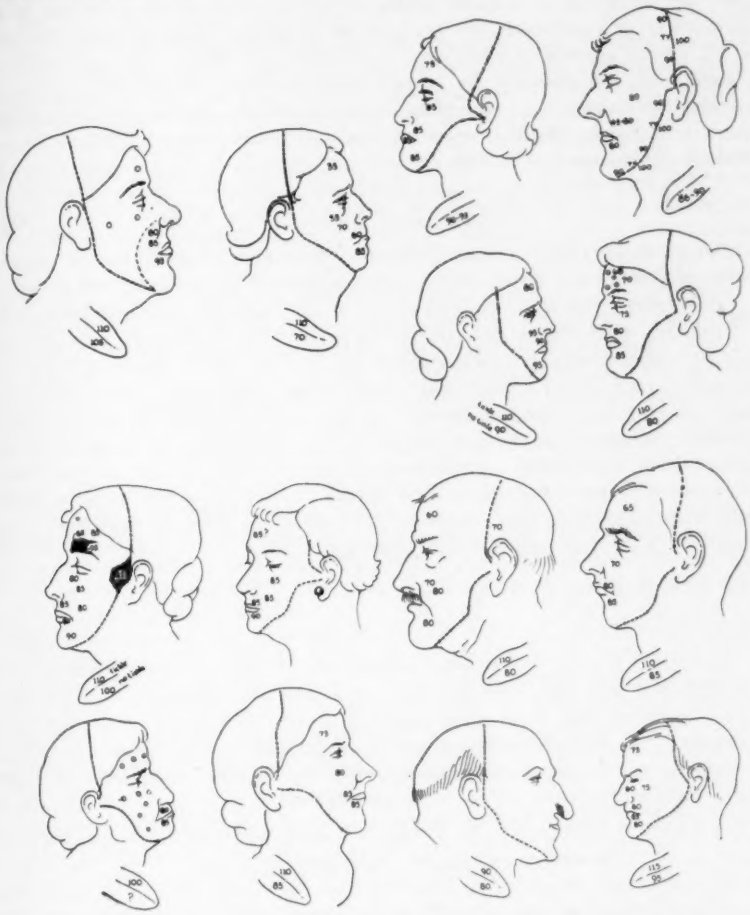
9. Gilmer, B. V. H.: The Measurement of the Skin to Mechanical Vibration, J. Gen. Psychol. **13**:42, 1935.

10. Davis, Loyal: The Deep Sensibility of the Face, Arch. Neurol. & Psychiat. **9**:283 (March) 1923.

11. Ivy, R. H., and Johnson, L. W.: Preservation of Deep Sensibility of the Face After Destruction of the Fifth Nerve, Univ. Pennsylvania M. Bull. **8**:15, 1907.

12. Maloney, J. W., and Kennedy, R. Foster: The Sense of Pressure in the Face, Eye and Tongue, Brain **34**:1, 1911.

anesthetic areas in fourteen patients in whom the sensory root of the fifth cranial nerve had been sectioned by Dr. Loyal Davis were explored with this vibrator (figure). In nine of these persons vibration sense was present in the areas supplied by all three branches of the nerve; in two, only about the upper and lower lips; in one, in a more extensive area supplied by the middle and lower branches, and in one, only in the tongue. In only one instance was the tongue on the side of the section insensitive to vibration.



Drawings showing anesthetic areas in fourteen patients in whom the sensory root of the fifth cranial nerve had been sectioned. Numerals indicate the position of the dial at which vibration was perceived. At the position of 80 vibrations of 55 cycles per second were produced; at 85, 77 cycles per second; at 90, 115 cycles; at 95, 150 cycles; at 100, 250 cycles; at 105, 310 cycles; at 110, 625 cycles, and at 115, 1,400 cycles.

Contrary to some other observers, I found the tongue exceedingly sensitive when stimulated with a vibrator of this type. On the normal side tickle as well as vibration was felt, but on the side of the section, only vibration. It is significant

that vibration sense was absent over part or all of the frontal bone in six cases, showing that stimulation of this type spreads by way of the underlying bone, is small and periosteum and bone possess less sensibility than other tissues.

Whereas on the normal side vibration of rapid frequency was felt, usually as high, for example, as that produced by oscillations of 625 cycles per second, or at times higher, on the side of the section oscillations of only from 4 to 150 cycles per second were felt. On the side of the tongue corresponding to the side of the section the most frequent oscillation felt was one of 250 cycles per second. The number of oscillations produced by the apparatus does not mean that there were a similar number of vibrations of the reed, since there were both production of harmonics and damping by contact with the skin. At this time I am not concerned with the actual frequencies of the oscillations felt but wish only to point out that, although vibration sense can be felt on the affected side, it is of a different order than that felt on the normal side.

CONCLUSION

From these observations I believe that crucial evidence is adduced of the existence of sense organs and pathways permitting the apperception of vibratory stimuli applied to the skin when epicritic and protopathic sensibilities have been destroyed. Whether the receptors reside in the skin or subcutaneous tissue cannot be stated, but it is suggestive that the area over the frontal bone with lesser amounts of subcutaneous tissue is less sensitive, at times not sensitive at all. Finally, although vibration sense of a certain character is preserved when epicritic and protopathic sensibilities are destroyed, a vibration sense of a different order is present when they are intact. This suggests that vibration sense consisting of apperception of repetitive stimuli may be carried from both epicritic and deep receptors.

25 East Washington Street.

DISCUSSION

DR. PAUL C. BUCY: I wonder whether Dr. Pollock is not measuring something different with this apparatus than one ordinarily measures with the tuning fork. I gathered that these were repetitive tactile stimuli, like those one would experience if one held the vibrating prongs of the fork against the skin and allowed it to vibrate rather than those obtained when the butt of the tuning fork is held against the skin or bone.

DR. LEWIS J. POLLOCK: As I said, vibration sense as I interpret it means apperception of repetitive stimuli of touch and pressure. When one places a tuning fork on an extremity, as illustrated by Katz when he placed an elbow on the vibrating box and felt vibration in his hand, one produces repetitive stimulation by waves. In this case I presume that the sensory nerve endings for deep sensibility were stimulated; when one applies a vibrating reed at the angle of the nose, one feels vibration and a tickle. In both instances I think one is dealing with vibration sense; psychologists now are concerned much more with examination of vibration sense through such a mechanism as a vibrating reed energized by an oscillator.

Abstracts from Current Literature

Physiology and Biochemistry

THE FORMATION OF PAPILLEDEMA. HANS LAUBER, Arch. Ophth. **13**:733 (May) 1935.

There are many theories concerning the formation of papilledema. Von Graefe and, later, Türck expressed the belief that it is caused by compression of the cavernous sinus by increased intracranial pressure, as a consequence of which venous stasis leads to swelling of the disk. Knape, Deyl and Dupuy-Dutemps modified the theory by presuming that compression of the central vein takes place at the entrance of the vein into the optic nerve or in the intervaginal space. Von Hippel said that the venous obstruction is necessary to the edema. Schmidt-Rimpler and Manz based their "transport" theory on the fact that there is open communication between the subdural and the subarachnoid spaces in the cranial cavity and about the optic nerve. Elschnig, however, pointed out that in bilateral papilledema the dilatation of this subdural space can be present on one side and absent on the other. Schieck, after anatomic examination in cases of fresh papilledema, stated that the cerebrospinal fluid acts by compression of the optic nerve superficially, or by dilating the perivascular lymphatic spaces in the optic nerve, and that it can prevent the circulation of lymph from the globe toward the cranial cavity, dilate the perivascular lymphatic spaces, compress the vessels and thus reach the disk, to push the cribriform plate forward into the globe. Jackson, Benedikt and Dor expressed the belief that edema of the optic nerve is the consequence of vascular irritation on a nerve basis. Parinaud, Ulrich, Sourdille, Klauber and Liebrecht claimed that edema of the brain spreads to the optic nerve and reaches the disk, in this way causing the edema. Gowers, Leber, Deutschmann and Elschnig stated that toxins in the cerebrospinal fluid are a factor in causing inflammatory changes. Behr claimed the existence of a system of lymphatic spaces throughout the optic nerve, through which liquid from the vitreous continuously flows toward the cranial cavity.

Recent observations and experimental facts support the idea that an increase of diastolic venous pressure in the retina and its relationship to the diastolic arterial pressure in the retina are decisive for the formation of papilledema. If arterial tension in the retina is low, even a slight increase of venous pressure caused by high intracranial pressure produces papilledema. In the presence of low arterial pressure, a venous pressure of from 28 to 30 mm. of mercury leads to hyperemia of the disk, with indistinct limits; in slightly higher pressures (35 mm. of mercury) the characteristic picture of papilledema appears. If, on the contrary, the diastolic arterial pressure is high, a venous pressure of 35 mm. causes no hyperemia of the disk; hyperemia appears when the pressure rises to from 40 to 45 mm., the picture of papilledema developing at a still higher pressure. In one case intracranial pressure amounted to 450 mm. of water, and venous retinal pressure was 50 mm. of mercury; yet the disk was only slightly hyperemic, and its limits were somewhat blurred. The arterial pressure in the retina was 130 mm. of water systolic and 85 mm. diastolic; the proportion of venous to arterial minimum pressure thus being 1:1.7. In all cases in which high intracranial pressure did not lead to papilledema, the proportion lay between 1:1.7 and 1:2.6. The alteration of the proportion to from 1:1.7 to 1:1.5 always led to hyperemia of the disk and blurring of its margins. Alteration of the proportion beyond 1:1.5 always led to papilledema.

An interesting point is the appearance of the disk in cases of low intra-ocular tension. Paton and Holmes showed that if there is any difference in the tension of the two eyes, papilledema is more marked in the eye with the lower intra-ocular

tension. It is known that general blood pressure has scarcely any influence on intracranial and intra-ocular pressure and that it does not influence retinal venous pressure. Retinal venous pressure, however, is about twice the height of intra-orbital venous pressure. From these facts one can deduce that the pressure of the cerebrospinal fluid in the intervaginal spaces of the optic nerve keeps the venous pressure of the retina at a comparatively high level.

The facts enumerated enable one to explain the formation of papilledema on the basis of a comparatively simple mechanism. Low diastolic blood pressure in the retinal arteries with normal intra-ocular tension and a simultaneous rise of retinal venous pressure are the main conditions leading to the formation of papilledema.

SPAETH, Philadelphia.

PECULIAR TYPES OF REFLEX-SYNERGIAS OBSERVED IN COMATOSE PATIENTS. CARL F. LIST, J. Nerv. & Ment. Dis. **83**:381 (April) 1936.

Reflex synergias are associated contractions of several muscle groups in one or more limbs induced by different kinds of afferent stimulation. They probably represent phylogenetically older neuromotor mechanisms. The complicated and varied motor responses in three comatose patients suggest that the cord alone is not sufficient to perform highly complex reflex action. Reflex synergias of the upper extremity have been classified as extension, or lengthening, and flexor, or shortening, reflexes. The prevailing influence of the more differentiated voluntary innervation of the upper extremities may account for the breaking up of the intimate connections of the primitive synergias, whereas the motility of the legs remains at a more primitive or phylogenetically older stage, showing the coordinated reflexes in a purer and more constant form.

The quality of the stimulus has some influence on the reflex response; thus, only nociceptive stimuli, such as pricking, pinching or exposure to extreme temperatures, produce the reflexes described, whereas proprioceptive stimuli are ineffective. There is an interesting relationship between the location of the stimulus and the type of reaction elicited. Riddoch and Buzzard found in cases of cervical tetraplegia that reflex action always appeared first in muscles belonging to the same spinal segment, the corresponding dermatome of which had been previously stimulated. The reflex then spread to adjacent higher and lower segments. In the observations by List, stimulation of the head, neck and upper extremities, except for the thumbs and palms, nearly always induced extensor movements, whereas irritation of the thenar eminences, the palms of the hands and all segments below the third dorsal caused flexion.

HART, New York.

AN INVESTIGATION OF THE NERVOUS CONTROL OF DEFAECATION. D. DENNY-BROWN and X. G. ROBERTSON, Brain **58**:256, 1935.

Denny-Brown and Robertson have attempted to define the activity of the rectum and the anal sphincter in "automatic defecation" and to analyze the nervous control of the evacuating mechanism in the normal subject and in conditions in which spinal reflex activity is present. Subjects with destructive lesions involving the sacral innervation of the rectum and anus were studied. Contraction of the rectum is attended by reciprocal relaxation of the anal sphincter. On the other hand, often no rectal contraction accompanies the long, slow, spontaneous fluctuation in the sphincter. The period of evacuation begins when the greatest increase in rectal pressure coincides with the greatest relaxation of the sphincter and declines only as the sphincter closes.

This reciprocal relationship between the rectum and the involuntary sphincter is a nervous mechanism. The adequate stimulus is tension on the wall of the rectum. Passive tension appears sufficient to bring about slight relaxation of the sphincter, but active tension is a more powerful stimulus. The nervous mechanism for this "reflex" appears to be related solely to the peripheral nerve plexus. When

the rectum and the sphincter are controlled by the central nervous system, their form appears to undergo only quantitative changes; the mechanism of these reactions may still be regarded as local.

The mechanism of automatic defecation is subject to depression by spinal shock for a brief period, during which the sphincter ani relaxes only slightly in response to passive distention of the rectum. Cutaneous stimulation in the cutaneous area of the sacral segments, with maximal effect at the anus, and activity of the bladder both facilitate the occurrence of reflex defecation.

The sympathetic nerve supply (hypogastric nerve) to the rectum and anus does not mediate these automatic and reflex responses. This was demonstrated in a patient in whom operative resection of the hypogastric nerves for the relief of megacolon had been performed. The behavior of the sphincter and rectum was normal except for a change related to increase in rectal capacity, which was present before operation.

The postural tone of the rectum and the sphincter ani is a reaction to passive tension of the muscle concerned. In each structure rapidly increasing tension causes tonic contraction to give way to phasic contraction; so tension is also the stimulus for phasic movement. The mechanism of postural tone of the sphincter ani is local and probably is related to the peripheral, i. e., intramural, nerve plexus. It is essentially unaffected as a result of a transverse spinal lesion, and the changes in the tonicity of the sphincter reflect only the degree of activity of the rectum and probably of the distal portion of the colon. Thus, in conditions in which the rectum is capable of active contraction and is distended, the internal anal sphincter is of low tone and is extremely plastic and soft to digital exploration. In the same cases evacuation of the rectum, the bladder or the pelvic portion of the colon brings about a return of high tone to the anal sphincter; there is, then, no obvious difference between one type of lesion and another. So also, when the normal subject has desire for defecation, the sphincter may be as patulous as that after a complete lesion of the cauda equina. The tone of the sphincter ani reflects the degree of activity of the rectum at the time of examination but its essential and particular mechanism remains identical whatever the nerve lesion. The commonly patulous sphincter in patients with established transverse lesions of the spinal cord and lesions of the cauda equina is therefore the clinical sign of the dyschesia from which they suffer. The mechanism of the tone of the sphincter is independent of the central nervous system.

Denny-Brown and Robertson demonstrated that after both a transverse lesion of the spinal cord and a lesion of the cauda equina fully developed automatic defecation can secure sufficient evacuation of fluids and that this reaction can be elicited from the rectum alone. The defective evacuation of solids resulting from these nerve lesions appears to result not from deficient reaction to distention of the rectum but from lack of sufficient propulsive power in the act. The deficiency is not an absence of peristalsis, which is as little evident in contraction of the rectum of the normal subject as in that of patients with these lesions. Defective evacuation appears to be related to the general force of contraction of the rectum, which is far greater in the normal subject when evacuating both fluids and solids, even when the abdomen is purposely maintained in a relaxed condition. Hurst (1921) attributed the lack of evacuation resulting from nerve lesions to lack of appropriate abdominal contraction, due to a defective sense of rectal distention; without doubt rises of abdominal pressure would stimulate the rectum and colon to earlier and more complete contraction. The authors believe that the force of contraction of the rectum is the primary factor, without which evacuation, even of fluids, is impossible. When this contractile process is lacking, as in patients with a recent lesion of the cauda equina or the conus, abdominal contraction is without effect, as in persons with inactivity of the rectum associated with primary dyschesia who are otherwise healthy.

Voluntary control over defecation extends directly only to the voluntary external sphincter. The function of micturition and that of defecation are almost

entirely comparable in their reaction to a transverse lesion of the cord. Their mechanism is almost identical except for the lack of any potent voluntary inhibitory control over the contractions of the rectum.

SALL, Philadelphia.

OBSERVATIONS ON THE NERVES OF SUPPLY TO THE BLADDER AND URETHRA OF THE CAT, WITH A STUDY OF THEIR ACTION POTENTIALS. JOSEPH P. EVANS, J. Physiol. **86**:396 (May 4) 1936.

The bladder of the cat is made up of a fundus and a long neck, extending in the male to the prostate and in the female to a bulbous muscular expansion, similarly situated. In each sex this segment of the urethra extending as far as the pelvic fascia constitutes the first portion of the urethra, and here lies the external sphincter. In the perineum lie certain "accessory sphincteric" muscles. The internal sphincter is represented by the neck of the bladder.

The tonic state of moderate contraction characteristic of the cat's bladder is accompanied by a constant outflow of impulses over the pelvic nerves to the filaments of the fundus.

Sudden reduction of intravesical pressure abolishes momentarily almost all nervous activity, though leaving a residual discharge which is associated with the contraction of the detrusor muscle on the escaping fluid contents.

The afferent impulses responsible for the reflex come from stretch receptors the activity of which is similar to that of stretch receptors in skeletal muscle.

The effective internal sphincter is the neck of the bladder. It receives its nerve supply from the pelvic nerve, as does the fundus, and the nature of the nervous activity is indistinguishable electrically from that of the fundus. The discharge to the fundus is definitely excitatory, and the available evidence suggests that the discharge to the neck of the bladder is inhibitory.

The external sphincter is characteristically maintained closed by a constant nervous discharge, which is inhibited reflexly when the intravesical pressure rises to a critical level, the inhibition depending on afferent impulses from the fundus carried over the pelvic nerves.

The immediate result of section of the pelvic nerve is disappearance of all postganglionic impulses to the bladder, but ten days or more after the section some discharge from the isolated ganglia can be detected. It is uncertain whether this discharge can ever become subject to reflex control and how far it regulates the activity of the "automatic" bladder.

It has been impossible to obtain evidence of a satisfying nature, under the conditions set up in this series of experiments, that the sympathetic system plays any part in the activity of the bladder.

ALPERS, Philadelphia.

THE ANTAGONISM BETWEEN CURARINE AND PROSTIGMIN AND ITS RELATION TO THE MYASTHENIA PROBLEMS. GRACE BRISCOE, Lancet **1**:469 (Feb. 29) 1936.

The beneficial effect of the injection of prostigmin in cases of myasthenia was first described by Walker. She was led to this important observation because of the resemblance between myasthenia and mild poisoning with curare and the well known antagonism between physostigmine, of which prostigmin is an analog, and curare. Pritchard demonstrated that the form of the myogram for patients with myasthenia differs markedly from the normal, showing quick fatigue with high rates of stimulation, and that prostigmin restores the myogram to the normal form, while simultaneously restoring the patient's strength. In this paper Briscoe shows that the quick fatigue which occurs with mild curarization can be restored to normal by a large dose of prostigmin, thus producing experimentally reactions similar to those observed in patients with myasthenia gravis.

Myograms were made, using the cat's quadriceps muscle. Myograms were first taken as controls, showing the responses to short spells (from one to two seconds) of stimulation of different rates and strengths. A small dose of curarine chloride was then injected intravenously. In a few minutes the contraction caused by the fast rate of stimulation was not maintained as in the myogram taken as a

control, but rapidly gave way. The myogram closely resembled that for patients with myasthenia taken in response to fast rates. At this point a large dose of prostigmin (1 cc. for a cat weighing 3 Kg. preceded by atropine) was given intramuscularly. In a few minutes the myogram improved and returned to normal. Experiments made as controls showed that recovery due to gradual elimination of curarine would take an hour or more.

The mode of action of the antagonism between prostigmin and curare was indicated by Briscoe by studying separately the peripheral actions of the two drugs on fresh, unpoisoned muscle. Myograms taken as controls showed that fast rates of stimulation produce larger contractions than slow rates. A few minutes after the intramuscular injection of prostigmin, a progressive change was seen in both the size and the shape of the myogram. The response to the fastest rate with strong stimuli was most affected, being both diminished in size and less well maintained, until eventually, at the end of from ten to twenty minutes, it was smaller than the response to the slowest rate and was twitchlike. In contrast to this, after moderate doses of curarine there was no fundamental change in the sizes of the contractions relative to each other. As in the control series, the faster rates of stimulation produced a larger contraction; that is, normal order was retained, though all the contractions were reduced in size and were twitchlike. This is in direct contrast to the condition following prostigmin poisoning.

On the basis of these findings, Briscoe offers two explanations. One supposes that the fault in curare poisoning and in myasthenia gravis lies in the too rapid destruction (or insufficient production) of the transmitter. A second explanation is that curarine counteracts the depressant effects of prostigmin not by affecting the output or stability of the transmitter but by raising the threshold for its depressant action when excess is present. WATTS, Washington, D. C.

SYNDROME OF DISEQUILIBRIUM AND ATAXIA OF FRONTAL LOBE ORIGIN (CEREBELLOVESTIBULAR PSEUDOMANIFESTATIONS); EXPERIMENTAL STUDY. A. AUSTREGESILO and A. BORGES FORTES, Encéphale **31**:1, 1936.

Amputation of one prefrontal lobe was carried out in four dogs. The resulting disturbances were evident as soon as the anesthesia wore off. There were lateral flexion of the head with slight torsion, scoliosis with concavity toward the side of the operation, ipsilateral hypertonia, contralateral hypotonia and titubating gait, with a tendency to fall toward the contralateral side. The animals walked in circles, the side of the lesion being toward the center of the circle. When the dog was rotated toward the side of the lesion, there was a tendency to straighten the body revealed by extension of the head. There was no nystagmus. When the dog was placed on the ground immediately after rotation, there was marked lateropulsion of the hind quarters toward the contralateral side. The radius of the circles described by the dog was diminished.

When the dog was rotated toward the contralateral side, there was flexion of the head with shortening of the trunk. There was no nystagmus. When the animal was placed on the ground, there was marked lateropulsion with falling toward the side of operation. The pelvic extremities were held widely separated. The radius of the circles described by the dog was much increased.

None of the dogs showed any paralysis. Tendon reflexes were more active on the contralateral side. In some cases there was ataxia of the anterior extremity on the side opposite the lesion. Some of the dogs had generalized convulsions for a few hours after operation. One dog had "mental disturbances with visual hallucinations and attitudes of anger." Anatomic study of the brains showed that the anterior frontal decussation (*carrefour*) was destroyed. Studies of the secondary degenerations will be reported in another paper.

One dog underwent bilateral frontal lobectomy but died in a few hours, with generalized convulsions and hyperthermia.

From these experiments, as well as from the clinical and experimental work cited from the literature, Austregesilo and Borges Fortes draw the following conclusions: In addition to its manifest psychic rôle, the prefrontal lobe regulates

and distributes the muscular tone of the contralateral side necessary for the maintenance of body posture and for orientation and equilibrium. The frontal lobe can be considered a superior vestibulocerebellar center.

LIBER, New York.

THE SYNKINESIAS. T. ALAJOUANINE and R. THUREL, Encéphale **31**:97, 1936.

Synkinesias are defined according to Vulpian as movements effected involuntarily in one part of the body at the moment voluntary or reflex movements take place in another. Synkinesias of coordination exist normally in the new-born child. After the age of 9 months they are gradually inhibited and replaced by new motor associations. This type of synkinesia is similar to a voluntary movement and, like it, involves reciprocal innervation with no tonic disturbance. In cases of hemiplegia synkinesias are unilateral, always on the paralyzed side. When they follow a movement of the same side they are termed ipsilateral. Examples are flexion of the entire lower limb following voluntary flexion of the thigh, extension following the corresponding movement of the thigh, the pronator sign and other reflexes. Imitative ipsilateral synkinesias are movements of the lower limb reproducing those of the upper, or vice versa. They occur only in conditions in which deep sensibility is disturbed, as in thalamic lesions. Thus, imitative movements which represent a normal tendency cannot be inhibited. Contralateral synkinesias follow corresponding movements of the nonparalyzed side. In cases of paraplegia synkinesias are bilateral. They are obtained by stimulation of the skin in a radicular territory below the level of the lesion. A whole chain of proprioceptive stimuli and motor responses can thus be set up. If the first reflex movement is prevented from taking place, the whole chain is suppressed. This occurs when the first response is prevented by ischemia of the muscles. Global synkinesias are contractions, or exaggerations of a preexisting pyramidal contracture, involving the whole paralyzed territory. They follow a voluntary act, an automatic act, such as sneezing, or a stimulus producing an effective change. Agonist and antagonist muscles are contracted at once, and voluntary movement is seriously interfered with. The tonic cervical reflexes of Magnus and de Kleyn are synkinesias in which movements of the head result in tonic changes of the limbs. Thus, turning the head away from the paralyzed side produces an increase of flexion contracture of the upper limb and a diminution of extension contracture of the lower limb, and vice versa. Motor repercussivity denotes the special reactivity of an excessively excitable center to any affective stimulus, regardless of its source. Its diagnostic value is the same as that of global synkinesia. It differs from hyperalgesic reactions. In the latter the motor response is diffuse and results only from stimulation of an excessively excitable peripheral territory. The reproduction by the preserved side of movements executed by the paralyzed side must not be regarded as synkinetic, as they can be inhibited voluntarily.

LIBER, New York.

INFLUENCE OF SURGICAL INTERVENTION ON AND APPLICATION OF DRUGS TO LABYRINTH ON BODY POSTURE AND MOVEMENT. R. THAUER and G. PETERS, Arch. f. d. ges. Physiol. **235**:316, 1935.

After careful unilateral labyrinthine extirpation in frogs typical asymmetry in posture develops slowly; it appears at once after intracranial severance of the eighth nerve or after injection of cocaine into the labyrinth. The delay in the development of the asymmetry is due partly at least to the stimulating effect of the operation, which counteracts the loss of the labyrinthine impulses. Other factors seem to play a part. This is indicated by observations after bilateral labyrinthectomy. If the second labyrinth is removed several minutes after the first, the asymmetry following the first operation persists in some cases for a time after the second labyrinthectomy. This is explained by the assumption of an after-effect of the first labyrinthectomy on the whole central nervous system.

SPIEGEL, Philadelphia.

Neuropathology

THE FAMILIAL FORM OF RETINITIS PIGMENTOSA WITH BLINDNESS AND OBESITY OF CEREBRAL ORIGIN (FIRST ANATOMIC OBSERVATION). L. VAN BOGAERT and P. BORREMANS, Ann. de méd. **39**:54, 1936.

The disease which is commonly known as the Laurence-Biedl syndrome is characterized by the association of adiposity and retinitis pigmentosa. Many other accessory malformations have been described: polydactylism, congenital cataract, congenital nystagmus, strabismus and deformation of the spine and skull. There is congenital retardation of mental development. Van Bogaert and Borremans describe the simultaneous occurrence of the syndrome in two brothers, the mother of whom suffered from keratitis and was mentally subnormal. In the first brother retinitis developed in early youth, and at the age of 10 years abnormal obesity was noticed. He died at the age of 29, of cardiac insufficiency. The only pathologic feature noticed at autopsy was symmetrical hyperostosis of the frontal bones, with adhesions of the dura mater. The brain was grossly normal, and sections through the region of the tuber cinereum did not show any histopathologic changes. There was, however, a peculiar necrosis with hyalinization of the center of the infundibulum. The anterior lobe of the hypophysis was intact. The second brother had visual disturbances at the age of 7 years and was mentally retarded. At present, at the age of 29, he shows dystrophia adiposogenitalis, with retinitis pigmentosa, cataract, rotatory nystagmus and brachydactylia.

WEIL, Chicago.

PROGRESSIVE UNILATERAL RIGIDITY WITH CHOREO-ATHETOSIS AND TORSION SPASMS ABOUT THE LONGITUDINAL AXIS. G. BOUCHE and L. VAN BOGAERT, Rev. neurol. **64**:886 (Dec.) 1935.

The illness began at the age of 10 years, during convalescence from acute rheumatic fever, and was characterized by contraction of the left foot associated with equinovarus, extending later to the arm, with marked hypertonus. The first torsion spasms began about five years after the onset of hypertonus. A few minutes before the onset of the spasm the patient felt vague uneasiness and excitement but remained conscious, and at times by energetic countersuggestion he could inhibit the attack. There was never biting of the tongue or loss of sphincter control, but he complained of intense pain in the mouth and the whole left side of the body. During the attacks the head turned to the right; the face became flushed; the eyelids contracted; the pupils dilated; the mouth opened wide, and the tongue protruded, covered with thick saliva. Meanwhile, the left arm became extended; the hand flexed and pronated on the wrist; the thumb became enclosed within the fingers, and extension of the leg and foot increased. The patient turned toward the right, and at the height of the crisis respiration was arrested. A few mild clonic movements and some erection of hairs over the shoulders, with profuse and generalized sweating, terminated the crisis.

The patient had these attacks for five years before succumbing to subacute bacterial endocarditis with septicemia. There were marked alteration in the heart and kidneys and an early stage of cirrhosis of the liver. The brain showed diffuse chronic meningo-encephalitis. There was an abiotrophic process in the globus pallidus, particularly on the right, with involvement of the external segments of the subthalamic bodies. It was characterized by diminution in the number of cells and marked reaction on the part of the glia, without much fibrillar gliosis and with minimal disturbance in the myelin pattern. The lesions were especially marked in the inner segments of the globus pallidus and the outer segments of the corpus subthalamicum. Nevertheless, the pallidosubthalamic connection showed little change. The cortical and subcortical lesions were probably not responsible for the condition.

FREEMAN, Washington, D. C.

STUDIES ON PATHOLOGIC NEUROGLIA IN MAN: II. SENILE DEMENTIA. GASTONE CANZIANI, Riv. di pat. nerv. **46**:409 (Sept.-Oct.) 1935.

Canziani investigated the histopathologic aspects of neuroglia in nine cases of senile dementia by the silver bromo-iodide method of Lugaro and reached the following conclusions: Neuroglial hypertrophy in senile dementia may reach the same intensity as in dementia paralytica but is not as constant. It may even be limited to partial hypertrophy of the isolated elements, which stand out in a mass of normal or partly hypertrophic astrocytes. There is no parallelism between hypertrophy and hyperplasia or between hyperplasia and atrophy of the cerebral tissue. Clasmatodendrosis varies from one case to another and possibly is related to factors not connected directly with senile dementia.

Canziani describes a degenerative process of the glia cell for which he proposes the name of reticulocystic degeneration. It consists in the formation in the cell of small, round cavities which tend to fuse in a grapelike manner, though maintaining their individuality. These formations presumably are related to an accumulation of lipoids.

Lesions of clasmatodendrosis observed in his material allow Canziani to divide the process into four stages: (*a*) cells showing dendrorhexis (dendrites in the process of fragmentation); (*b*) atypical cells, in which swelling is established in the fragmenting dendrites; (*c*) ameboid cells, in which the swollen fragments become transformed into pseudopodic expansions, and (*d*) corroded cells, in which the process has disappeared and the protoplasmic body undergoes a process of progressive corrosion.

FERRARO, New York.

NEW ADVANCES IN THE KNOWLEDGE OF CLASSIC NEUROGLIA AND OLIGODENDROGLIA IN "STATUS EPILEPTICUS": SIMILARITY OF ALTERATIONS OF THE NEUROGLIA CELLS AND THOSE ENCOUNTERED IN EXPERIMENTAL CATATONIA. G. P. RODRÍGUEZ PÉREZ, Arch. de neurobiol. **15**:71, 1935.

Recently, Rodríguez Pérez published a preliminary report of the results obtained in the study of the neuroglial elements in patients with epilepsy who died in a state of grand mal and described the existence of a special type of neuroglial disintegration, distinct from the clasmatodendrosis of Ramón y Cajal, which he designated as microclasmositosis. This is a type of fine disintegration of the body and the glial prolongations. Pérez does not consider this histopathologic picture pathognomonic of epilepsy. Later investigations with Sanz showed that an identical degenerative process is observed in experimental guanidine intoxication and in the catatonia produced by bulbocapnine.

Pérez thinks that microclasmositosis may be a specific destructive process due to agents of the toxic-vascular type. Recently, he studied another case of epilepsy and presented newly acquired data. He noted advanced processes of neuroglial disintegration which might represent the final state of microclasmositosis. The cytoplasm of the neuroglial cell showed hydropic degeneration, with multiple vacuoles filling the cell body and finally causing complete destruction of the gliocytes. The vacuoles were separated from one another by strands of protoplasm with fine aurophilic granules, similar to those existing in the prolongations. It is usual to find spongy and vacuolar degeneration of the protoplasm occurring in the glia cells a little after the fine granular fragmentation of the prolongations.

Recently Pérez, working with Gorriz, produced experimental catatonia with convulsions with pure bulbocapnine. On examining the neuroglia cells after death, he observed degenerative phenomena identical with those described in cases of status epilepticus.

ALPERS, Philadelphia.

THE RELATIONSHIP BETWEEN TAY-SACHS' AND NIEMANN-PICK'S DISEASE, WITH SPECIAL REFERENCE TO THE BIOCHEMICAL MECHANISM OF THE PROCESSES. K. VON SANTHA, Arch. f. Psychiat. **101**:593, 1933.

Santha insists on the difference between amaurotic family idiocy and lipoid histiocytosis both on a morphologic and on a biochemical basis. According to

Spielmeyer and Bielschowsky, there is accumulation of prelipoid and lipoid substances in the cell plasma, which secondarily, through imbibition of water, causes swelling of the cell. However, Schaffer expressed the belief that the prelipoid materials are deposited in the primarily swollen plasma. Shaffer also claimed that Tay-Sachs' and Neimann-Pick's disease are phenotypically different disorders. In Tay-Sachs' disease there is elective involvement of the neural parenchyma, spreading from the cerebral cortex to the sympathetic ganglion cells, whereas in lipoid histiocytosis there is involvement not only of the neural elements but of the connective tissue, especially of the histiocytes throughout the body. There may be involvement of the glial elements in cases of amaurotic idiocy. The two diseases are similar in that histochemically lecithin is present in the cells. The greatest difference between the two diseases has been shown by Epstein. In the brain affected with Niemann-Pick's disease there is a surplus of 80 per cent of ether-soluble phosphatides of the lecithin group, while in amaurotic idiocy there is no increase in the phosphatides. The material from patients with the latter condition, however, had been subjected to formaldehyde fixation for a number of years; it has been shown that formaldehyde reduces the phosphatide content. It seems that breaking down of the molecule of phosphatide gives rise to numerous smaller molecules with greater endosmotic tension, causing imbibition of water. Finally, from each consideration it appears that Niemann-Pick's disorder is an example of simple infiltrative lipoidosis, while Tay-Sachs' disease, as indicated by the chemical findings, is fatty degeneration rather than lipoidosis.

FREEMAN, Washington, D. C.

CHANGES IN THE SPINAL CORD IN A CASE OF "RECOVERED" FUNICULAR MYELOSIS. L. BOUMAN and MAX BIELSCHOWSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:538 (April) 1935.

Bowman and Bielschowsky report the anatomic changes in the case of a man who recovered clinically from pernicious anemia and died of carcinoma of the stomach twelve years later. During the earlier period of hospitalization he complained of pain in the limbs and chest. These were the only clinical changes indicating neural involvement at that time. Examination of the spinal cord did not show the spongy appearance characteristic of pernicious anemia. Stains for myelin sheaths showed irregularly distributed areas of demyelinization, which were most marked in the posterior and the lateral column. The changes usual in cases of combined sclerosis were not present. The axis-cylinders were intact, and the myelin sheaths, though present, were smaller and narrower than those usually observed in the part of the cord examined. Glial proliferation was also noted in this area.

These histopathologic changes are regarded as evidence of a tendency to healing of lesions of the cord associated with pernicious anemia. The authors conclude, therefore, that the changes in the spinal cord are reversible. This is the first case in which anatomic evidence of healing within the cord is recorded. Degeneration of the myelin sheaths is usually the earliest pathologic change in pernicious anemia. Cerebral changes were observed in this case. They were due not to pernicious anemia but to arterial occlusion.

SAVITSKY, New York.

INTRACRANIAL LIPOMA: CASE OF MENINGEAL LIPOMATOSIS ASSOCIATED WITH MICROGYRIA. EUGEN SCHERER, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**: 45 (Oct.) 1935.

Scherer reports the only case of a flat lipoma over the convexity of the cerebral hemisphere recorded in the literature. Intracranial lipoma is most often encountered in the region of the corpus callosum or in the middle fossa. It is usually composed entirely of fatty tissue intimately related to the pia and its vessels. Occasionally formation of bone is observed in the fatty mass. The tumor is usually incidentally noted at autopsy. It rarely gives rise to clinical changes because of its unusually slow growth.

A woman aged 51, whose birth and early development were normal, had had epileptic attacks since her second year. She was backward at school. The attacks were not present from between the ages of 11 and 14 years. At the age of 24 she was admitted to a hospital, where she was described as disoriented and retarded, with frequent generalized convulsions preceded by an aura in the right hand. At that time she had weakness of the lower part of the face on the right and paresis of the right upper limb but no speech defect. From 24 to 40 years of age she remained in the hospital, where she deteriorated progressively. Generalized convulsions were frequent until death.

Autopsy revealed a large yellowish tumor, the size of the palm of the adult hand, over the temporoparieto-occipital region of the left hemisphere. It was in the leptomeninges and was covered by arachnoid. It was most definitely developed in the temporo-occipital part of the convexity. The occipital pole was spared. The mass extended to the superior part of the parieto-occipital region, extending slightly to the medial surface. Small fatty masses were present throughout the meninges, even at the base, especially near the anterior edge of the temporal lobe. The meninges were thickened throughout, presenting a milky-white appearance, especially in the more posterior parts. The posterior half of the left side of the brain was definitely smaller than the right. The left frontal region appeared relatively large. The brain weighed 925 Gm. The white substance was markedly reduced, especially in the occipital region and somewhat less in the parietotemporal region. The tumor was composed of purely fatty tissue, with a maximal thickness of from 5 to 6 mm. The posterior and the middle cerebral vessel on the left appeared definitely altered and rigid as they passed through the thickened meninges and fatty tissue.

Microscopic study of the tumor confirmed its fatty nature. It was not richly vascular. The tumor tissue rested on the thickened pia and was covered externally by a thin fibrous capsule, which fused with the arachnoid. No tumor tissue penetrated the sulci, which were closed by proliferating connective tissue. The subarachnoid space at the site of the tumor was practically obliterated except for occasional clear spaces near the sulci, containing coagulated fluid. The larger blood vessels were thickened.

The temporo-occipital convexity in the region of the lipoma showed microgyria. There were four instead of six cellular layers. The granular layer of the normal cortex was absent. Except for occasional loss of ganglion cells, the normal architectonic arrangement of the cortex was not disturbed. The microgyric part of the cortex was filled with calcific bodies, which were most numerous in the upper layers. These bodies lay free in the brain tissue, at times displacing ganglion cells. Small calcareous deposits were also noted along the capillaries. The staining reactions of these concretions resembled the pseudocalcific deposits in the globus pallidus, which are considered to be colloidal precipitates with an attraction for calcium.

Marginal gliosis was present. The connective tissue around the blood vessels entering the cortex was increased. The white substance of the posterior half of the brain, especially in the temporo-occipital region, was degenerated. Especially affected were the periventricular pathways in the region of the posterior and the inferior horn, such as the optic radiations and the inferior longitudinal fasciculus. The calcarine fibers were also markedly involved. There was diffuse isomorphous gliosis in this area of degenerated white matter. There was no fat, which pointed to the conclusion that the demyelinating process was long standing. Typical sclerosis of the left cornu ammonis was present. There was some dropping out of Purkinje cells, with storing of lipoid pigments in the ganglion cells of the dentate nucleus and the olives.

The lipoma in this case probably began in early childhood and interfered with the development of the underlying cerebral hemisphere. The microgyria and the lipoma may be associated anomalies, though their close proximity in the brain suggests an intimate pathogenetic relation. Scherer accepts Wassermann's conception that cerebral lipomas arise from proliferation of cells in the adventitia of pial vessels.

SAVITSKY, New York.

FREQUENCY AND CLINICAL SIGNIFICANCE OF CEREBRAL METASTASES OF MALIGNANT GROWTHS, ESPECIALLY PRIMARY PULMONARY NEOPLASMS. WOLFGANG BRUNNER, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:793 (Feb.) 1936.

Brunner found 1,781 malignant tumors in 12,025 successive necropsies performed at a hospital in Munich, between 1920 and 1933; in 127 (7 per cent) of these cases the tumor was a primary neoplasm of the lung, and in 74 (4.2 per cent) cerebral metastases were shown. Of the intracranial metastases, 28 (37.8 per cent) were from the lung, 12 (16.1 per cent) from hypernephromas, 23 from carcinomas in other parts of the body and 11 from primary sarcomas. Cerebral metastases were shown in 28 (28.2 per cent) of the 99 cases of pulmonary neoplasm in which the brain was examined, in 12 (16.9 per cent) of 71 cases of hypernephroma, in 23 (1.6 per cent) of 1,473 cases of other carcinoma and in 11 (9.9 per cent) of 114 cases of sarcoma. Twenty-one of the 28 cerebral metastases from a pulmonary tumor caused cerebral symptoms (75 per cent), and 23 (50 per cent) of 46 cerebral metastases from other types of tumor. Twelve (43 per cent) of 28 metastases to the brain from the lung and 7 (15 per cent) of 46 other tumors caused cerebral symptoms alone. In 5 cases of primary tumor of the lung in which there were cerebral metastases a diagnosis of primary tumor of the brain was made. In only 1 case of the other tumors in which there were cerebral metastases was such a diagnosis made.

The tumors of the lung arose from the larger bronchi in 30 per cent of the cases, most often near the hilus and usually in the upper lobe (75 per cent). These tumors were mainly on the right side. The metastases varied from solitary lesions the size of a large apple to multiple lesions the size of a pea. They were usually softened and necrotic in the center, and varied from yellow white to grayish and hemorrhagic. Sixty-five per cent of the cerebral metastases were in the left hemisphere and were localized with decreasing frequency in the following parts of the brain: the occipital lobe, the frontal lobe, the cerebellum, the parietal lobe and the temporal lobe. In only 1 of 28 cases was meningitis carcinomatosa observed.

Brunner notes the importance of knowing the frequency with which carcinoma of the lung metastasizes to the brain and states that often the pulmonary signs may not be evident during life. The picture presented may be that of a primary tumor of the brain. Brunner urges a thorough investigation for a primary malignant focus in every case of tumor of the brain. A roentgenogram of the lung should be taken in every case before operation is advised.

SAVITSKY, New York.

A CASE OF NUCLEAR APLASIA OF MOEBIUS COMBINED WITH ARHINENCEPHALY. A. BIEMOND, Acta psychiat. et neurol. **11**:49, 1936.

Biemond describes the case of a child who since birth presented ptosis of the left eyelid, slight convergent strabismus, with paresis of vertical movements of the left eye, and peripheral paralysis of the right facial and accessory nerves. The child died at the age of 10 months of bronchopneumonia. Postmortem study of the brain revealed incomplete development of the circle of Willis, absence of the right vertebral artery, agenesis of both olfactory nerves and hypoplasia of the commissural systems of the forebrain (rostrum corporis callosi, commissura anterior and anterior crus fornicis). The secondary olfactory centers (gyrus hippocampi, cornu ammonis and gyrus dentatus and their fiber systems), the hypothalamus with its fiber systems, the commissura posterior, the psalterium, the fimbria and the splenium corporis callosi were fully developed. Serial sections of the brain stem and the medulla revealed hypoplasia of the upper portion of the left oculomotor nucleus (for the levator palpebrae muscle), the roots of both trochlear nerves and the nuclei of the abducens and the facial nerve bilaterally. Only a trace of the nucleus of the accessory nerve, with a slender root, was present on the right side, whereas on the left neither the nucleus nor the root of the eleventh nerve was present. The hypoplastic nucleus of the hypoglossal nerve was presented by a single (unpaired) mass of cells situated in the median

line of the medulla. The posterior longitudinal bundle was somewhat thin, but all other tracts, including the lemnisci, the pyramidal tracts, the pontile fibers and the bundle of Schütz, were normal. Biemond points out the significant coincidence of aplasia of the motor nerve nuclei, with agenesis of the primary rhinencephalic centers, and the developmental defect in the vascular system of the base of the brain. Because the olfactory nerves, the anterior portion of the corpus callosum, the fornix and the anterior commissure develop from the lamina terminalis, which, in turn, is formed by occlusion of the neuropore at the anterior end of the neural tube, one may regard arhinencephaly as a result of malocclusion of the neural tube in this place. Biemond is inclined to believe that the disturbing influence in the normal course of formative processes in the ventral and oral areas of the neural tube originates in the ventrally situated entodermal and mesodermal embryonal structures. He points out developmental defects of various entodermal and mesodermal organs repeatedly observed in cases of arhinencephaly (syndactyly and congenital defects of the heart and kidneys). In the case reported such a mesodermal defect was significantly represented by the anomaly of the arterial circle of Willis. Biemond concludes that the ventrally situated anlagen of the motor nuclei in the neural plate were affected directly by disturbances in the development of the mesoderm, whereas the olfactory nerves and the commissural systems were involved indirectly, as the result of an impediment in the process of occlusion of the oral end of the neural tube.

YAKOVLEV, Waltham, Mass.

Psychiatry and Psychopathology

MENSTRUAL DYSFUNCTIONS IN DISORDERS OF THE PERSONALITY: THEIR NATURE AND TREATMENT. EDWARD B. ALLEN, Endocrinology **19**:255 (May-June) 1935.

Allen investigated one hundred and fifty patients at the Bloomingdale Hospital, White Plains, N. Y., who suffered from functional mental illnesses, in an attempt to determine the relation of menstrual disorders to mental disturbances. There were fifty-four cases of schizophrenia, fifty-four of manic-depressive psychosis, twenty-one of psychoneurosis and twenty-one of a miscellaneous group of conditions, made up of psychopathic personalities and psychoses associated with somatic disease. The ages varied from 14 to 50 years. The results of Allen's study show that only the emotional factor appears to have a definite correlation both qualitatively and quantitatively with variations in menstrual functions. Allen believes that a depressive mood, physical depletion and motor underactivity are conducive to amenorrhea. On the other hand, an expansive, elated or excited mood with motor overactivity predisposes to a profuse and prolonged menstrual flow. Agitation and worry are more likely to be associated with a profuse than with a diminished flow. Improvement in the general health and relief from emotional distress were productive of the best results in menstrual dysfunction associated with disorders of the personality. In no case did endocrine therapy directly shorten the period of amenorrhea or increase a diminished menstrual flow. The substances used were theelin and progynon by intramuscular injection, ovarian extract orally, amniotin intramuscularly and a combination of ovarian extract, corpus luteum and thyroid extract by mouth. In cases of dysmenorrhea or prolonged menstruation antuitrin-S offered subjective relief and appeared to diminish the flow but did not shorten the duration of the period.

PALMER, Philadelphia.

MENTAL RETARDATION ASSOCIATED WITH ENDOCRINE AND NON-ENDOCRINE CONDITIONS. M. B. GORDON, L. KUSKIN and B. BERKOWITZ, Endocrinology **19**: 561 (Sept.-Oct.) 1935.

Gordon, Kuskin and Berkowitz report on the mental status and related data of 958 children. They divide the material into endocrine and nonendocrine groups. The former comprises 529 children presenting evidences of childhood myxedema

(which term the authors prefer to sporadic cretinism), hypothyroidism, adiposogenital dystrophy in boys, thyropituitary obesity, anterior pituitary growth deficiency, goiter, hypogonadism and gigantism. There were 429 children in the nonendocrine group. As all but 29 of these were mentally retarded, this group is referred to in this paper as the "non-endocrine mental retardation group." The disorders include postencephalitis, congenital syphilis, epilepsy and an unclassified group and various other nonendocrine conditions.

The purpose of the study was to determine the part played by the endocrine dyscrasia in a large group of children with mental retardation; the mental status of children with the individual endocrine diseases, the relationship of mental status to developmental growth, as manifested by the time of onset of teething, walking and talking for children with both endocrine and nonendocrine disturbances; the relation between mental retardation, endocrine disease, illness and trauma, and the relation between congenital syphilis, endocrine disorder and mental retardation.

Fifty per cent of the children with endocrine disorders were of normal mentality, and the other 50 per cent were retarded, an intelligence quotient of 80 being used as the critical value. Mental retardation occurred with the greatest frequency in association with the following diseases in the order named: childhood myxedema, hypothyroidism, pituitary obesity (adiposogenital dystrophy and thyropituitary type), anterior pituitary growth deficiency and goiter. Mentally retarded infants with endocrine conditions were found to cut teeth, walk and talk at a later date than mentally normal infants in the same endocrine groups. Practically all children with childhood myxedema in this series were mentally retarded and showed delay in all developmental fields. In the authors' experience, mental retardation, irrespective of its etiology, is associated with a delay in both physical and mental development if the mental retardation occurs during the first year of life. There was a greater tendency for mental retardation associated with childhood myxedema and hypothyroidism to appear in the first two years of life. Mental retardation in association with disturbances of the pituitary gland appeared to a greater extent after the second year of life. A concomitant appearance of mental retardation and endocrine dyscrasia was found to the greatest extent in cases of childhood myxedema, to a lesser degree in cases of hypothyroidism and to the least extent in cases of disturbances of the pituitary gland. Mental retardation occurs more frequently after an acute illness in association with a disturbance of the pituitary gland and hypothyroidism than with childhood myxedema. A history of trauma is present in the pituitary group only and in not a single instance in the thyroid class in this series. Congenital syphilis played an insignificant part in the production of endocrine disorder (5.5 per cent). The incidence of congenital syphilis was only 8 per cent in the nonendocrine group of mental retardation.

On the basis of their findings, the authors are unable to state definitely the etiologic relationship between endocrine disease and mental retardation. The subject should be studied further under uniform and controlled investigative methods. The authors suggest that every child with mental retardation should be studied from a comprehensive point of view.

PALMER, Philadelphia.

ORGANOTHERAPY IN MENTAL RETARDATION ASSOCIATED WITH ENDOCRINE AND NON-ENDOCRINE CONDITIONS. M. B. GORDON, L. KUSKIN and J. AVIN, Endocrinology **19**:572 (Sept.-Oct.) 1935.

In this paper Gordon and his co-workers report the effects of treatment by organotherapy of children suffering from mental retardation. They have limited the study to 317 mentally retarded children who were under observation for at least one year. Signs and symptoms of endocrine dyscrasia were present in 155 and manifestations of mental retardation of nonendocrine origin in 162 children. Organotherapy consisted of the administration of desiccated thyroid and pituitary substance in various doses and combinations. Thyroid gland was given by mouth

in an initial dosage of 1/10 grain (0.006 Gm.) twice a day for the first week and three times a day for the third week. No medication was given during the second and fourth weeks. This alteration was adhered to with an increase in dosage every month to 1/8, 1/4, 1/2 and 1 grain (0.008, 0.016, 0.032 and 0.065 Gm.). When the 1 grain dose was reached, the therapy was discontinued for the fourth week. In some instances thyroid was given twice a day for the first week of each month and three times a day for the second and third weeks. In a few instances the maximum dosage was increased to 2 grains (0.13 Gm.) three times a day. The authors have found in the past twenty years that this cautious method of treatment affords an adequate check on intolerance and overdosage. In former years whole pituitary substance was administered by mouth, but this has been changed in the past five years to desiccated anterior lobe of the pituitary gland as a better standardized product. The initial dose of the latter is 1 grain three times a day, which is increased every month by 3 grains (0.19 Gm.) a day until 5 grains (0.32 Gm.) three times a day is reached. The pituitary preparation is given three times a day for the first three weeks of each month and then discontinued for the fourth week.

In children with adiposogenital dystrophy, thyropituitary obesity or hypogonadism, extract of the anterior lobe of the pituitary gland or the anterior pituitary-like gonadotropic hormone from the urine of pregnant women is given by hypodermic injection, 1 cc. twice a week. In addition to organotherapy, remedial measures were attempted to eliminate malnutrition, focal infections, orthopedic conditions, defective vision, disturbances of hearing and speech, carious teeth and constitutional diseases, such as syphilis, tuberculosis and rickets. Diets were generously supplied with vitamins, minerals and proteins. Educational measures were undertaken in muscular coordination, sense training and academic study. Social conditions were studied by several agencies, and attempts were made to remedy faulty situations by cooperative efforts of school authorities and social and medical agencies.

In an evaluation of the therapeutic values of each of these measures, the authors believe that diet, improvement in social conditions and elimination of physical disabilities had no effect on the mental status in any child in the series. The change in mentality is due, they believe, to organotherapy or to the educational measures. The part played by the latter is great, but since practically all of the children of school age, especially those of lower mentality, had the benefit of a more or less standardized educational program, it must be concluded that any beneficial results are to be attributed to the effects of glandular preparations. The results obtained were: A tendency to continued improvement was observed in 45 per cent of the group with endocrine disorders and in 1.2 per cent of the group in which mental retardation was not associated with endocrine disturbances. In the former group fair or temporay results were obtained in 34 per cent and poor results in 21 per cent, while in the latter group fair or temporary results were obtained in 34.6 per cent and poor results in 64.2 per cent. A tendency to continued improvement following the administration of desiccated thyroid and pituitary gland was noted only in cases of mental retardation which were associated with endocrine disorders. The highest incidence was noted in cases of deficiency of the anterior lobe of the pituitary gland, childhood myxedema, hypothyroidism and pituitary obesity, in the order named. Better results (58 per cent) were obtained in the children with thyroid disturbances than in those with hypopituitarism (30 per cent). According to the experience of the authors, the administration of desiccated thyroid and pituitary glands will neither cure nor tend to produce a continuous improvement in mental retardation associated with nonendocrine conditions. The most that can be expected are fair or temporary results. It is concluded that in the treatment of associated endocrine and nonendocrine disturbances, organotherapy can be expected to produce an improvement in endocrine symptoms but not in mental retardation or in the nonendocrine condition.

PALMER, Philadelphia.

SEX DIFFERENCES IN DREAM CONTENTS. RICHARD W. HUSBAND, J. Abnorm. & Social Psychol. **30**:513 (Jan.-March) 1936.

An attempt was made to study the content of dreams in two groups of persons: twenty-five men and twenty-five women, all with normal personalities and of college age. The direct interview method was utilized, subjects in each group being interviewed by some one of the same sex, though the same questions were applied to all. A few married persons were included. Few of these fifty subjects had studied enough psychology to understand the possible interpretation of their dreams. The results as tabulated in statistical form were roughly: Exactly the same number of men and women, fourteen in each group, dreamed more than once every week. Three times as many women as men experienced dreams accompanied by the emotion of fear, whereas dreams of pleasure occurred in almost the inverse ratio. Twelve men as compared with five women reported dreams of pleasure. Almost twice as many women as men dreamed of personal worries. Consistent with this was the fact that almost twice as many women as men dreamed of topics about which they were thinking before retiring. Emotional states which beset the women influenced them to twice the extent that they did the men, whereas physical stress operated on the men's dreams four times as often as it did on the women's. Almost the entire group of women, twenty-three of twenty-five, dreamed of being pursued, and twenty, of falling, whereas no men dreamed of the first and only eight of the second. None of the group of men dreamed of drowning, murder or torture, whereas six, eleven and seven women dreamed of these three subjects, respectively. Almost twice as many men as women dreamed frequently on the topic of future events, whereas the women were inclined to dream more often of past events. Twenty of the twenty-five men never dreamed in terms of color; fifteen women stated that color was frequently noted in the dream content. There was no large discrepancy between the two groups in the frequency of dreams connected with sex. There was no significant disparity between the two groups in the number who had sex dreams of a major form, such as actual sexual relations—twenty-one men and twenty-one women. However, far fewer men dreamed of the milder forms of sexual activity, such as kissing—only sixteen, as compared with the entire group of women. Perhaps as a corollary to this, almost half of the women told of often waking excited after a dream, whereas only 12 per cent of the men admitted doing so. Concerning the subjects of the dreams it was learned: The men dreamed chiefly of casual acquaintances, whereas most of the women dreamed more frequently of good friends; the sexual dreams of the women were directed to a particular person who was absent and was being missed at the time. The object of the men's sexual dreams was more impersonal; only three said that their dreams of sex tended to appear when they were missing a particular person. The great majority of women found that their dreams were more frequent and vivid when there was lack of sexual excitement. Eight women dreamed of rape and six of exhibitionism, while only two men dreamed of the latter. The number of men with dreams of an incest character as compared with the number of women was in the relation of 5:2.

Husband's conclusions are: The dreams of married persons are fewer and involve less sexual content than those of single persons. Women dream about "boy friends," while men do not so often dream about "the girls they care for." Women's dreams are much more vivid and emotional and contain more elements of fear.

WISE, Howard, R. I.

PSYCHOLOGICAL FACTORS IN THE ETIOLOGY OF DIABETES. WILLIAM C. MENNINGER, J. Nerv. & Ment. Dis. **81**:1 (Jan.) 1935.

Menninger studied twenty-two patients with mental disorders associated with diabetes. A review of the literature suggested that the psychic factor of emotion is still an involved problem. Few observers state definitely that diabetes may be psychologic in origin, though many are agreed that it may be aggravated by

emotional factors. Menninger is struck by the inconsistency of the opinion that psychogenic factors are of great importance once the diabetes is established but not in initiating the metabolic disorder.

In ten of the twenty-two cases of mental disorder in his series the diabetes developed in apparent synchronism. In five cases the diabetes developed in the course of the mental disorder, and in seven the diabetic condition was recognized before the onset of the mental disturbance. In twelve cases of the entire group paranoid delusions were shown as an outstanding mental symptom.

Studies of the heredity in the cases both of diabetes and of mental disorder were unreliable. Much is yet to be learned about diabetes by further study of the psychologic influence, which has been consistently neglected by investigators interested in the more tangible physicochemical aspects of the problem. Study of the twenty-two cases in his series convinces Menninger that there is close parallelism between the metabolic and the mental disturbance.

HART, New York.

THE BLOOD FATS IN SCHIZOPHRENIA. ARTHUR T. BRICE, J. Nerv. & Ment. Dis. **81**:613 (June) 1935.

Brice concludes from a study of a group of patients with hebephrenic, paranoid and catatonic forms of dementia praecox that there is evidence of depression of the level of the fatty acids and the cholesterol of the blood in schizophrenia and that the functions of desaturation and utilization of fatty acids seem to be closely associated with motor phenomena. He believes that there is correlation between variation in the absolute levels of cholesterol and unsaturated fatty acids in the blood and variation in the emotional state. The depression of this level seems most marked among the apathetic, stuporous patients. He concludes that further study of the unsaturated fatty acids of the blood in cases of schizophrenia is desirable.

HART, New York.

REACTIVE PSYCHOSIS IN RESPONSE TO MENTAL DISEASE IN THE FAMILY. LAURETTA BENDER, J. Nerv. & Ment. Dis. **83**:143 (Feb.) 1936.

The concept of the reactive psychogenic psychosis owes much in its development to the American school of psychiatry. Hoch argued against any sharp line dividing organic and psychic factors in the production of mental disease. Glueck and White emphasized a special category of reactive psychoses not conforming to the manic-depressive or the dementia praecox group and related to strong emotional experience. Bender reports case histories in eleven family groups in which psychosis developed in one member probably because of a psychosis in another. Cases of this sort are differentiated from those of *folie à deux* by the fact that there is no imitation of the first psychosis in the latter condition and that the identification processes in reaction psychosis are not intellectual, as in *folie à deux*, but emotional and determined specifically by the family relationship. In three of the cases reported there was a brother-sister group, in three, a sister-sister group; in three, a mother-daughter group, and in two, a mother-son group. There were no father-sons groups in the study.

Constitutional similarities between members of the same family, only one of whom may show outspoken psychotic behaviorism, are often conspicuous. Brothers, sisters, mothers and fathers are often as suspicious, secretive and uncooperative as the patient suffering from evident paranoid disease. Psychic mechanisms of identification or aggressive feelings toward the patient or the "in-laws," with ideas of guilt, play a large part. Misunderstood sexual difficulties, problems of masturbation, disturbance in the security of the home and break-up of a personal relationship play an important rôle. The incest motive in these cases is not brought out clearly by the author. There are the prevalent feeling that the psychosis in one member of the family is an indication of weakness in the family stock and, consequently, the natural fear that the same fate may overcome others. Charac-

teristic is the unwillingness to accept the situation. It is not to be expected that the reactive psychosis will take the same form as the constitutional psychosis that precipitated it. Schizophrenia in one member of the family does not necessarily precipitate schizophrenia in another member but leads more usually to some form of anxious depressive state. There may, however, be definite schizoid coloring in the reactive depression of such a person. This does not make the prognosis in the reactive psychosis more serious, even if the other member suffers from a deteriorating process. There is a tendency for imitative features, which are probably less due to constitutional similarities than to identification processes. One mother clings to her psychosis, while she remains more or less contentedly in the same hospital with her schizophrenic son. Recovery from the reactive psychosis is possible, even when the first member of the family does not recover from his or her psychosis. It is remarkable that in the group studied the reactive psychoses were in women, whereas the initial mental illness in the family was more or less equally divided between men and women. This would suggest that women are more closely tied up emotionally with the family relationship and are less well adjusted on a heterosexual basis. There were no instances of daughters reacting to a psychosis in the mother or the father. It is interesting that the reactive psychosis seems to occur in response to a mental breakdown in a member of the family who stands for a double function in the family. Thus, a sister reacted psychologically after a brother became mentally ill, when the father was dead and the brother had played the emotional rôle to the sister of both a brother and a father. In another case the sick sister came to represent the dead father, who was more beloved than the husband. In this case recovery came with a closer attachment to the husband. In another case the younger sister represented all the family and emotional ties of an older sister, who had no hopes of marriage. The threat of marriage of the younger sister and a toxic psychosis with threat of death precipitated a bewildered depression in the older sister. In all cases in which the mother reacted to mental disease in a child, whether a daughter or a son, the father of the child was dead. In the mother-daughter situation the mother appeared dissatisfied with her own life and had hoped her daughter would live a purer life. The mother-son relationship was simpler than the mother-daughter situation. The son came to stand for the dead father, even when the mother had married again.

In general the prognosis in the reactive psychosis is good and depends on two factors: (1) recovery from illness of the beloved relative, and (2) specific psychotherapy directed toward an understanding of the psychic mechanisms involved.

HART, New York.

PSYCHIATRIC ASPECTS OF MYXEDEMA. ANDREW J. E. AKELAITIS, J. Nerv. & Ment. Dis. **83**:221 (Jan.) 1936.

Diminution in the functional performance of the entire organism results from insufficiency of the thyroid gland, with diminution of excitability of the vegetative nervous system and psychic retardation. Myxedematous swelling of the skin, an expressionless, swollen face and general stupidity of appearance are characteristic. Speech is monosyllabic. There is loss of initiative, so that the patient sits immobile for hours at a time. Fatigue and ready exhaustibility after slight exertion are common. Patients are likely to become depressed and irritable. Orientation and memory for remote events are usually not impaired. Headaches in the frontal and occipital regions occur. The patients may pass into stupor, which may last for months.

It is important to differentiate between a coincidental psychosis occurring during myxedema and a mental disturbance arising during the myxedema and dependent on it. The differentiating test is apparently the response to the administration of thyroid extract, which, if given to a patient with independent psychosis, will not cause improvement. Wagner von Jauregg concluded that 15 per cent of

patients with myxedema are psychotic. The psychosis usually arises when the myxedema is advanced. Patients described by Kraepelin, Pilcz and Wegener showed repression, ideas of persecution, nihilism, hallucinations, clouding of consciousness and a peculiar form of affective disturbance which Wegener designated as resigned anxiety. Akelaitis considers most cases reported in the literature to be of the delirious-hallucinatory reaction type; he describes two cases, both of women, aged 58 and 41 years, respectively, in which such a mental picture was shown. Both patients showed increase in dextrose tolerance, puffiness of the skin, loss of hair and a markedly diminished basal metabolic rate. There is described the case of another woman aged 52, who was in a myxedematous stupor, and a fourth case of an unmarried woman aged 66, in whom myxedema developed spontaneously in 1931; a year later the latter complained of depression and fatigue. After vigorous thyroid medication she became confused and more deeply depressed, later becoming clear and rapidly more cheerful.

HART, New York.

HALLUCINATIONS IN PSYCHOSES. JOEL M. HILL, J. Nerv. & Ment. Dis. **83**:405 (April) 1936.

This study consists of an investigation of the hallucinatory content and outcome of the illness of 100 male patients with psychoses. About 415 hallucinations wer recorded during a period of two years. The following classifications based on a dynamic understanding of the patients' hallucinations is proposed:

A. Hallucinatory defense against a sense of guilt or inferiority
  1. Projection of accusing or threatening conscience
     (*a*) Paranoid type without punishment expressed
     (*b*) Paranoid type with punishment expressed
     (*c*) Depressive type without punishment expressed
     (*d*) Depressive type with punishment expressed
  2. Confirmation of self-esteem by:
     (*a*) Projected approving conscience
     (*b*) Voices of friendly impersonal interest
     (*c*) Projection of responsibility

B. Endopsychic perception

C. Hallucinatory wish fulfilment
  1. Frank wish fulfilment
     (*a*) Sexual hallucinations
     (*b*) Erotic wishes toward incest objects
     (*c*) Hostile wishes toward others
  2. Disguised wish fulfilment
     (*a*) Sexual hallucinations with punishment expressed
     (*b*) Sexual hallucinations without punishment expressed
     (*c*) Resembling fairy-tales

D. Undetermined

The cases were classified according to the standards of the American Psychiatric Association. Hallucinations were more frequently associated with dementia praecox and least often with manic-depressive psychoses. Of the 415 hallucinations the special senses were involved as follows: hearing, in 282; sight, in 56; body sensations, in 44; smell, in 19, and taste, in 14. Visual hallucinations seem to have the best prognosis. The sooner the hallucinations develop after the onset of the psychosis, the better is the prognosis.

HART, New York.

QUANTITATIVE DREAM STUDIES: A METHODOLOGICAL ATTEMPT AT A QUANTITATIVE EVALUATION OF PSYCHOANALYTIC MATERIAL. FRANZ ALEXANDER and GEORGE W. WILSON, Psychoanalyt. Quart. **4**:371, 1935.

From the detailed records of interviews and reported dreams of patients with organ neuroses, Alexander and Wilson have attempted a quantitative evaluation of the amount of various genital and pregenital tendencies in a given person. This study is an attempt to make an economic analysis of psychoanalytic material, an approach which has remained so far much less reliable than the structural and the dynamic. The material is analyzed on the basis of intaking, elimination and retaining trends.

The dreams of eighteen patients whose analyses lasted from eight to twenty-four months were studied. The conclusions are: (1) In patients with peptic ulcer there are intense intaking tendencies, both passive receiving and aggressive taking. These tendencies are reacted to with an unusual amount of conflict. These patients also react frequently with compensating giving. (2) In patients with chronic diarrhea there are intense passive intaking tendencies, which produce severe conflicts resulting in marked compensating giving of a greater degree than that in peptic ulcer. Thus, patients with this disorder resemble those with peptic ulcer, but there is a real difference in the behavior: Patients with peptic ulcer compensate for this receptivity with actual efforts and those with diarrhea through symptoms. (3) Patients with constipation have strong retentive tendencies and aggressive elementary urges. Because of their projection mechanisms, they show less conflict than the other two groups, and they do not incorporate as much in their dreams, although they retain more. PEARSON, Philadelphia.

A PSYCHOANALYTIC OBSERVATION ON ESSENTIAL HYPERTENSION. LEWIS B. HILL, Psychoanalyt. Rev. **22**:60 (Jan.) 1935.

No therapy has been found to be consistently effective in modifying essential hypertension, though a variety of treatments have been reported to produce transient reduction. It has often been assumed that there might be a "nervous" element in such functional disturbances. In general the vasomotor system is unstable in its behavior in many persons with neuroses. Neurotic blushing and palpitation of this kind, however, do not lead to essential hypertension. "Nervousness" is not sufficient to explain symptoms. One must be able to relate the particular symptomatic disturbance to a definite emotional situation. Furthermore, one must show the causal relations between the one and the other to be able to deduce a convincing pathologic theory. In the light of freudian studies of the etiology of psychoneuroses, one might anticipate that a psychogenic hypertension can appear only when three conditions are met: A factor specific for this disorder but not of itself necessarily producing it; nonspecific factors causing stress, and the final insult leading to the appearance of symptoms.

The case reported is of interest because it contributes to an understanding of the relation of constitution and experience to the formation of symptoms. In a man aged 32 essential hypertension had been discovered fourteen years before, in the course of examination for participation in athletics. The family history was striking; it showed a marked tendency to cardiovascular diseases with hypertension, both organic and essential. Examination at the age of 18 years revealed that in the absence of any other disorder, the blood pressure was 180 systolic and 120 diastolic. During fourteen years blood pressure readings, taken from time to time, varied from 155 to 190 systolic and from 95 to 120 diastolic, the average being 170 systolic and 110 diastolic. When the patient came for psychotherapy there had developed tension and anxiety in an acutely difficult situation, which, on analysis, was shown to be related to the material later brought out. Clinical cure resulted from brief therapy, and the psychoanalysis was not completed.

Therapy followed the psychoanalytic method, with emphasis on emotional catharsis. During one treatment hour the patient dramatized a scene which occurred after his eighth year. He appeared to lose consciousness and then built up a rage reaction, at the height of which he grasped a weighted ash receiver and made a convincing attack on the analyst's head but actually avoided hitting him. His verbal offerings at this time were addressed to his mother. As his rage increased, he grew red in the face. As the scene ended he was pallid and sweating. For a brief time thereafter he was amnesic for the episode but was able to recall it by free association. His retrospective account of the memory which this cathartic experience released was that as a child he had been teased by his sister till he struck her. His mother, as a punishment, took a pony whip with the evident intention of striking him. This was unusual, the whip merely happening to be at hand. In his fear he seized it from her hand and ran from her, and he was brought to bay as he stood on a bed, intending to hit her with it. He lost courage and as a final act of surrender, with the hope of avoiding the whipping, merely handed the whip to her. She struck him angrily. He had forgotten the experience completely.

A short time after this analytic experience, the blood pressure was reported to be 145 systolic and 90 diastolic, and in the three years since this time it has never read over 135 systolic and 90 diastolic. Frequently it is 125 systolic and 85 diastolic. There was no other treatment which could have affected the blood pressure or change in his habits of living. There was nothing in the rest of the psychotherapy which seems to have any bearing on this condition.

KARPMAN, Washington, D. C.

A NOTE ON SUICIDE. MELITTA SCHMIDEBERG, Internat. J. Psycho-Analysis **17**:1 (Jan.) 1936.

Suicide can be looked on as a tendency to prevent oneself from committing forbidden acts. In other cases the decision to kill enables the subject to commit forbidden acts for which suicide is an atonement. Suicide always aims at hurting some loved person. It is not the death instinct which drives a person to suicide but more especially the feeling of anxiety which interferes with the instinct of self-preservation. The strongest incentives to suicide are fear of death and fear of life. Suicide is an escape from the real and fantasied dangers of life into a state of security and happiness. When a man kills himself, he hopes for a happier life after death. There are two ways of preventing suicide: making life more attractive or taking away hope in a future life.

Playing truant or running away in the case of children is a common substitute for suicide, stimulated directly by paranoid fears. Every action which implies giving up an old life and starting a new one, especially obsessional traveling, sexual promiscuity and prostitution, breaking off an analysis and going to prison, are unconsciously linked with suicidal fantasies. The same is true of fainting, hysterical fits and various ways of denying reality. Sleep and physical illness may be substitutes for suicide.

KASANIN, Chicago.

STUDIES ON THE INFLUENCE OF EMOTIONS ON THE FUNCTIONS OF THE ORGANS. ERICH WITTKOWER, J. Ment. Sc. **81**:533 (July) 1935.

This article is really a monograph of about 150 pages, with an extensive bibliography. The aim of the research was to learn how functional organic processes can be essentially altered by emotional influences. The material consisted of more than 500 observations in cases of disturbances in respiration and vascular, gastric and intestinal neuroses, with special consideration of the importance of psychologic factors in these conditions.

Wittkower finds that the size of the heart can be influenced by emotional factors. Both enlargement and diminution of the cardiac shadow occur in the roentgenogram. The dimensional changes sometimes amount to more than 1 cm. When the emotion fades, the cardiac changes recede.

Salivary secretion can be influenced by emotion, with a resulting increase or decrease in secretion. The direction of reaction is independent of the type of the emotion experienced. The thiocyanate and nitrogen contents of the saliva may increase or decrease under emotional influence. This is due to an increase or a decrease in the total quantity of saliva and not to concentration or dilution. In emotion saliva of different composition is produced.

Gastric secretion and motility can be influenced by emotion. Changes occur in the acidity, the quantity secreted and the emptying time of the stomach. All possible variations of disturbed gastric function occur. Emotional stimuli can cause extreme hyperacidity or even achylia refractory to histamine. The same emotions cause uniform changes in the same subjects and different changes in different subjects. Even under the influence of disgust, an increase in secretion and acidity may occur. The form of reaction does not depend on the type or intensity of the emotion; it seems to be determined typologically. Different emotions in the same subject always cause uniform changes.

The effects on the salivary and the gastric secretion are similar. There are persons who have an increase in salivary and gastric secretion with every type of emotion (plus types) and others who always have a decrease (minus types). These plus and minus types do not coincide with the visceral types of Eppinger and Hess; they coincide, rather, with the constitutional types established by E. R. Jaensch and W. Jaensch.

On the basis of a clinical observation, in which it was possible to cure intense gastroptosis by psychologic methods, the behavior of normotonic stomachs under emotional influence was investigated. In relief pictures of the mucosa it could be demonstrated that remodeling of the relief can be effected by puckering of the gastric wall, in a manner analogous to relief pictures of the gastric wall which have hitherto been interpreted as gastritis. In the majority of cases an increase of tonus was observed on emotional stimulation.

The stimulating effect of most emotions on the secretion of bile was demonstrated. Anger occupies a special position. During anger the flow of bile is entirely, or almost entirely, inhibited.

Wittkower finds that under emotional influence an increase in the leukocyte count generally takes place, more rarely a decrease. This affective leukocytosis occurs without change of the differential blood picture.

The occurrence of electrolytic changes under emotional influence has been proved. Changes in the calcium, potassium and chloride contents of the serum were observed. The water content of the blood can also be influenced by emotion. Under the influence of emotion the iodine content of the blood rises. Values for iodine were found such as are seen only in exophthalmic goiter. After the emotion has faded out, the iodine level drops gradually to the normal.

KASANIN, Chicago.

THE DEVELOPMENT AND DISORDERS OF TIME PERCEPTION. A. M. MEERLOO, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:231 (July) 1935.

Meerloo designates as the primitive time sense the ability to localize a particular moment within a temporal continuum. He brings evidence from the animal world of this type of time perception, such as the awareness of periodicity in fishes when they come up to be fed at certain times. Man has lost this ability to perceive the lapse of time without instruments of precision except in sleep, hypnosis and the rhythmic bodily functions. This primitive time sense is disturbed in cases of senile dementia and encephalitis epidemica. The inversion of sleep rhythm is a well known manifestation of the latter disorder. The ability to get up without a watch at night or at an early hour is a result of this primitive time sense. Alcohol and morphine interfere with this property of the organism.

The ability to measure the passage of time is poorly developed in man. Feeling tone plays an important rôle. When a person is bored, the same unit of time seems long. At other times, as during periods of anxiety, it seems short. Time

seems longer in the dark. To patients with exophthalmic goiter time seems shorter than it is and to patients with chronic encephalitis, longer. Children are able to measure short intervals of time fairly well, but long ones not at all. As the year goes on intervals of time seem shorter. The periodicity of exogenous stimuli determines to a certain extent the perception of time. Manic patients think the unit of time is short, while patients with a depression consider it long. Such disturbances of time perception are also observed in patients with cardiac arrythmia. A patient with angina pectoris felt that a few moments were everlasting. The ability to evaluate the lapse of time is defective in sleep and in dreams. Time seems prolonged during impending catastrophe.

The gnostic time sense is the arrangement of experiences in their proper chronologic sequence. A disorder of this type of time perception is most clearly seen in the Korsakoff symptom complex, in which memories are not lost but the temporal relations of past events are poorly conceived. It is sometimes seen in early stages of dementia senilis. Many so-called defective memories are really disorders in this modality of time perception. In dream distortions one sees most glaringly distorted gnostic elaboration of time experience.

Meerloo calls attention to the experience of the continuity of time. He refers to the perception of time as continuum rather than as a temporal juxtaposition of discrete moments. This feeling of continuity with the past and of merging with the future is a function of the ego. The transmutation of temporal experiences into a flowing continuum takes place automatically. Conscious effort to delimit a unit of time and to describe statically a given period in an individual life is a schematic arbitrary breaking up of such a continuum. Disorders of this type of time sense are seen in schizophrenia, the hypnogogic state, the déjà vu experiences in cases of lesions of the temporal lobe, chronic encephalitis and dementia paralytica. Under the influence of hashish and cocaine there is a feeling of unhampered movement in time.

One often encounters difficulties in grappling with problems of time in psychoneurotic patients. Some always seem to be wrangling about time. They either feel enslaved to the inevitability of the movement of time or find it necessary to regulate their lives strictly by the clock. Others avoid reviewing the past and facing the future. They live in the present and seek to take advantage of the fleeting moment. Some psychoneurotic persons either regret faux pas of the past or dread the future. The person with a compulsion neurosis is perpetually clashing with such problems. The present seems to play an insignificant rôle in the mental content of these patients.

SAVITSKY, New York.

Diseases of the Brain

LECTURES ON MOTOR ANOMALIES OF THE EYES; FUNCTIONAL NEUROSES: ETIOLOGY, PROGNOSIS AND TREATMENT OF OCULAR PARALYSIS. ALFRED BIELSCHOWSKY, Arch. Ophth. **13**:751 (May) 1935.

This article deals almost wholly with the treatment of muscular disturbances of the eye. Bielschowsky emphasizes the frequency with which spastic disorders of the ocular muscles are encountered in cases of hysteria. He thinks that, since the corresponding innervation is governed by the will, spastic movements can be learned by exercise and initiated by suggestion. This includes blepharospasm and convergence spasm, sometimes alone and at other times associated with accommodation and contraction of the pupils.

He has seen hysterical conjugate deviation. Nystagmus of hysterical origin is rare in his opinion and never the only symptom of hysteria. It is almost always accompanied by spasm of the orbicularis muscle and the muscles of convergence. The nystagmoid movements are exceedingly fine and rapid—much more rapid than in any other type of nystagmus. He also describes the so-called dissociation of ocular movements as a sign of hysteria. It was first described by Kunn as follows: "The eyes are not held rigidly in any certain position as in real spasms,

and they do not obey the patient's will but move about rather irregularly, one eye independent of the other as in a comatose condition." The supposition that conjugate movements of the eyes can be temporarily suspended in hysteria is a contradiction to all physiologic and clinical facts on which the general validity of Hering's so-called law of association of movements of the eyes is based. It is beyond one's volitional power to innervate either an individual muscle of the eye or the muscles of one eye alone. The occurrence of unilateral or asymmetrical movements of the eyes by no means proves that these movements arise from asymmetrical innervations of the two eyes. Further, the reception by the eyes of two simultaneous innervations, one impelling the eyes to a parallel movement and the other impelling them in an opposite direction, resulting theoretically in an asymmetrical or a unilateral movement of the eyes, cannot on critical examination be accepted. Bielschowsky thinks that in any case of hysteria in which there are apparently unusual motor anomalies of the eyes one must take into consideration the various possibilities of origin, particularly the coincidence of simple heterophoria and hysterical spasm and other possible organic lesions.

SPAETH, Philadelphia.

TROPHIC LESIONS IN MULTIPLE SCLEROSIS. CHARLES M. BYRNES, J. Nerv. & Ment. Dis. **82**:373 (Oct.) 1935.

Gowers, Marburg and Oppenheim agreed that nutritional disorders of the skin, hair and nails are rare in cases of disseminated sclerosis. Levinger reported hypertrichosis and Cans elephantiasis, but Ormerod seems to have furnished the only record of an ulcerated eruption of the skin in this disease.

Byrnes describes the case of a woman aged 21, whose first attack of the disease occurred in the summer of 1924 and the fourth in 1927, when she had complete paralysis of both lower extremities, diplopia, retention of urine, thick and hesitating speech and numbness of the trunk and lower extremities. Examination revealed temporal pallor of the disks, weakness of the external rectus muscle of the right eye, nystagmus, lower segment facial paralysis of the left facial nerve, slow, hesitating speech, exaggeration of the tendon reflexes and absence of superficial reflexes. In addition, there were marked weakness and incoordination of the upper extremities. Five days after her admission to the hospital two small bed sores developed over the sacral region. A few days later two small, thin-walled, painless blisters appeared on the flexor surface of the right thigh and the lateral surface of the left leg. These developed into raw, ulcerated areas. The lesion was thought to be trophic in origin.

HART, New York.

"CROWDING" OF EXCITATION AS THE IMMEDIATE CAUSE OF SOME EPILEPTIC FITS. MAX LEVIN, J. Neurol. & Psychopath. **16**:256 (Jan.) 1936.

In epilepsy there is undue excitability of parts of the brain, just as in narcolepsy there is an undue inhibitability. In some cases of epilepsy seizures are provoked by anger under circumstances necessitating the suppression of aggressive impulses. During the effort accompanying such suppression, "crowding" of excitation from the substrate of the aggressive movements to the remaining part of the motility substrate occurs. This leads to increase in tension, resulting in the discharge. The same mechanism may explain the seizures observed in dangerous situations, when the impulse to escape them is suppressed.

N. MALAMUD, Ann Arbor, Mich.

CEREBRAL ABSCESSES: DIAGNOSIS AND TREATMENT. P. PUECH, C. ELIADES and H. ASKENASY, Ann. de thérap. biol. **9**:1 (June-July) 1935.

Abscess of the brain has its origin in infection of the mastoid or the paranasal sinuses, direct injury of the brain and metastatic foci. Abscess is not infrequently multiple and is caused chiefly by Streptococcus, Pneumococcus or Staphylococcus.

It begins with an area of diffuse cellular infiltration, which later breaks down to form a cavity that tends to become encapsulated and even may heal. In diagnosis there are three considerations: the presence of an abscess, its location and its stage of evolution. There may be symptoms of generalized intracranial hypertension and, possibly, a focus (mastoiditis) that gives a clue to the localization; furthermore, there may be signs of infection, such as fever and leukocytosis. Features peculiar to cerebral abscess are intermittent headache, sometimes localized, and bradycardia; apathy and somnolence are frequent, with profound and rapid alteration of the general state. Chronic abscess usually causes no fever, and there may be little or no cellular reaction in the cerebrospinal fluid. In rare cases the abscess may be evident with roentgenography, usually on account of gas-forming organisms or calcification of the capsule. Ventriculography may be required for localization. Of great importance is the diagnosis of the stage of the abscess, since to intervene before the abscess is localized and encapsulated means almost certain death. A metastatic abscess tends to encapsulate most rapidly and an otitic abscess most slowly. Gentle exploration of the suspected area with a blunt needle is probably the best way of determining the condition of the wall of the abscess. Differential diagnosis from a tubercle, extradural and subdural abscess and posttraumatic serous meningitis may present difficulties.

The most satisfactory way of treating an abscess is dissection en bloc, without rupturing the capsule. Before this stage occurs, drainage must be resorted to, but operation on the abscess itself should be delayed at least until pus is present. Wide decompression may save the brain from serious damage during the period of diffuse suppurative encephalitis. Ordinarily mortality from cerebral abscess is from 70 to 75 per cent; in the series reported by Professor Vincent eight patients were treated by radical extirpation without death from infection, although two patients later succumbed on account of poor physical condition.

FREEMAN, Washington, D. C.

CLINICAL EXPERIMENTS WITH MCQUARRIE'S PITRESSIN TEST. H. P. STUBBE TEGLBJAERG, Acta psychiat. et neurol. **10**:595, 1935.

Teglbjaerg performed the pitressin test in sixteen patients with rare epileptic seizures. In three of four patients with cryptogenic epilepsy seizures were induced. Two of five patients with traumatic epilepsy had a single seizure. In only one of seven patients with atypical epilepsy was a suggestion of an attack produced. The author concludes that the test has a practical value in patients with rare seizures when direct observation of the attack is of diagnostic importance.

YAKOVLEV, Palmer, Mass.

INVESTIGATIONS ON EPILEPSY AND WATER METABOLISM. H. P. STUBBE TEGLBJAERG, Acta psychiat. et neurol., 1936, supp. 9, p. 1.

This study is based on an investigation of patients with epilepsy carried out for three years. After a preliminary chapter on the pathophysiologic features of the epileptic seizure, with considerable emphasis on the convulsive threshold and the water balance, Teglbjaerg discusses in detail water exchange in the organism. It is important that only about one-half the total supply of fluid is represented by what are ordinarily called beverages and that less than half the fluid is excreted through the kidneys and feces. Therefore, consideration of other sources and other modes of excretion of water must be undertaken in any careful study of water balance. In testing the theories of water balance advanced by McQuarrie and by Fay, Teglbjaerg leans toward that of the former—that epilepsy is a cellular manifestation rather than one of gross pressure. He repeated the dehydration experiment under controlled conditions, with reduction in the number and severity of the seizures.

The results of experiments on water balance are illustrated by charts of the behavior of the patients and tables showing the composition of the diets in terms

of the number of grams not only of carbohydrates, fats and proteins but of salts and free and "oxidation" water. The experiments were carried out on ten patients with epilepsy and nine persons used as controls. Reactions to a sudden change from an ordinary diet to dehydration were as rapid in the group of patients with epilepsy as in that of normal persons. The number of seizures was reduced in this period, but they were not eliminated. In a second period, when the fluid intake was increased excessively, the patients with epilepsy responded with diuresis as quickly as normal persons, but there was a marked increase in the frequency of the seizures. The mental state of the patients was also affected; so the experiments were discontinued. Throughout the experiments the patients with epilepsy showed greater instability in weight, daily excretion of urine, levels of blood chemistry and hematocrit determination.

Determination of insensible perspiration was carried out by means of the Sauter balance. It was found that the amount of insensible perspiration was not influenced by the epileptic seizure. The curves were somewhat irregular, but the amounts before and after an attack were the same. Teglbjaerg therefore concludes that the possible connection between epilepsy and water balance does not manifest itself in any conclusive changes in the amount of insensible perspiration.

Examination of the cerebrospinal fluid showed that the pressure was normal between seizures; it rose during epileptic seizures, parallel with the anoxemia. Injection of a hypertonic solution of sodium chloride or a hypertonic solution of dextrose modifies the blood volume and the cerebrospinal fluid pressure to only a slight degree, if at all. Teglbjaerg concludes that the epileptic seizure is not accompanied by any gross changes in the water balance of the organism. However, seizures that are elicited by hyperhydration have always been characteristic of individual patients, a fact indicating that a focus specific in these patients is irritated by his state. "For this reason I find it adjusted to seek an explanation of the connection between epilepsy and water metabolism in focal cellular conditions in the central nervous system."

FREEMAN, Washington, D. C.

Vegetative and Endocrine Systems

BASOPHILIC HYPERPLASIA OF THE PITUITARY IN ESSENTIAL HYPERTENSION. IRVING PARDEE, Am. J. M. Sc. **190**:1 (July) 1935.

Cushing demonstrated that hyperactivation of the neurohypophysis by hyperplasia of the basophilic cells and invasion of the posterior lobe of the hypophysis is the rule in certain types of hypertension. Two cases are presented to prove this point. A man aged 32 with a hypertensive plethoric syndrome characteristic of pituitary basophilism showed at autopsy a basophilic hyperplasia of the hypophysis. The second case was that of a man aged 37 with a group of signs characteristic of the basophilic syndrome. The necessity of studying further the pituitary-adrenal-diencephalic complex as a basic cause for hypertensive states is indicated.

MICHAELS, Boston.

STRUCTURAL CHANGES IN THE PITUITARY OF THYROIDECTOMIZED RATS. I. T. ZECKWER and others, Am. J. M. Sc. **190**:145, 1935.

When thyroidectomy is performed in young rats it results in a stunting of body growth, an increase in weight of the pituitary gland due to an increase both of solids and of fluid content, a marked reduction or nearly complete disappearance of acidophils, an increase in the number of basic-staining cells and the appearance of great numbers of large cells filled with hyaline substance. These "thyroidectomy cells" appear, according to the special staining technic used, to be transformed cells containing blue granules. The "thyroidectomy cells" appear to be secreting and storing a secretory product which is hyaline in appearance. It is suggested that the stunting of body growth in the cretin rat may be due to the loss of acidophils of the pituitary, which in turn depends on loss of the thyroid secretion.

Acidophils seem to disappear by degranulation rather than by frank degeneration. An abundance of thyrotropic hormone was found to be present in the pituitary glands of persons with cretinism in which there was depletion of acidophils, an observation which rules out the acidophilic cell as the producer of thyrotropic hormone. Since there is no atrophy of the adrenals in cretin rats, it is reasonable to consider that the acidophils cannot be the producers of the adrenotropic hormone. When thyroidectomy is incomplete, such changes are slight or absent.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

EXPERIMENTAL GASTRIC EROSIONS FOLLOWING HYPOTHALAMIC LESIONS IN MONKEYS. E. C. HOFF and D. SHEEHAN, Am. J. Path. **11**:789, 1935.

Of sixteen monkeys subjected to hypothalamic injury five showed multiple hemorrhagic erosions in the mucosa of the body of the stomach. The animals showed striking individual variations in the general postoperative condition. Those with gastro-intestinal lesions showed a disinclination to eat; their condition became progressively worse, and in three experiments death supervened within from twenty-four to forty-eight hours. In all cases the erosions were confined to the stomach, none occurring in the duodenum. The erosions were multiple and hemorrhagic, entirely confined to the mucosa, and some showed a punched-out appearance. In three of the five experiments in which gastric erosions were present the stomachs showed considerable dilatation and atony, suggestive but not conclusive evidence of sympathetic activity. Histologic examination of the hypothalamic injuries revealed that in all the animals showing gastric erosions at autopsy the lesions were small and confined to the tuberal nuclei. In only one of the five was the track of the injury hemorrhagic. Positive evidence is therefore advanced to show that histologically verified lesions, confined to the tuberal nuclei and leaving all other hypothalamic nuclei intact, may lead to hematemesis and multiple mucosal erosions in the body of the stomach. In a control series of over fifty monkeys subjected to many and varied types of nonhypothalamic cerebral lesions, careful postmortem examination of the gastro-intestinal tract revealed only one animal with gastric or duodenal ulceration, and this animal had been subjected to bilateral motor and premotor extirpation five months prior to being killed and to transections of the spinal cord at the sixth thoracic and the third cervical level five weeks and twelve days, respectively, before autopsy. The consistently negative observations in the control experiments appear to lend greater significance to the association of gastro-intestinal lesions with injury of the hypothalamus or interruption of descending autonomic pathways.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

RELATION OF THE CUSHING SYNDROME TO THE PARS INTERMEDIA OF THE HYPOPHYSIS. W. G. MACCALLUM, T. B. FUTCHER, G. L. DUFF and R. ELLSWORTH, Bull. Johns Hopkins Hosp. **56**:350, 1935.

A typical case of the Cushing syndrome is described, with symptoms and anatomic changes corresponding with those already known. The cells of the tumor are cylindric and arranged radially about capillary blood vessels. In their form these cells resemble those of the pars intermedia and are different in form and arrangement from the basophilic cells of the anterior lobe. Furthermore, on staining by a method described by Cowdry employing copper acetate and hematoxylin, it is observed that, while the basophils of the anterior lobe are stained black, the cells of the tumor, like those of the pars intermedia, including those which radiate into the posterior lobe, remain unstained. For these reasons and because of its continuity with that tissue, it is concluded that the tumor is derived from the cells of the pars intermedia. If this is true, the remarkable disturbances of function which accompany the presence of this tumor, most of which have been thought dependent on some change in the anterior or the posterior lobe, may rouse new interest in the activities of the pars intermedia.

FROM THE AUTHORS' CONCLUSIONS. [ARCH. PATH.]

AUTONOMIC FACIO-CEPHALALGIA. RICHARD M. BRICKNER and HENRY ALSOP RILEY, Bull. Neurol. Inst. New York **4**:422, 1935.

Four cases of pain in the head and face are described. All presented striking evidence of involvement of the autonomic nervous system. The similarity between this disturbance and some so-called atypical neuralgias is discussed, and the term "autonomic faciocephalalgia" is suggested in place of "atypical migraine" or "atypical neuralgia," on the assumption that the autonomic disturbance is the basic causative factor and is primarily responsible for the production of the attacks, since the pain was readily relieved by the administration of epinephrine in two cases and by gynergen in the other two. It is assumed that such attacks are due to localized hypofunction or hyperfunction of the sympathetic nervous system. In cases of hypofunction epinephrine is effective, while gynergen is of value in states of hyperfunction.

KUBITSCHEK, St. Louis.

STUDIES ON OVARIAN DYSFUNCTION. F. ALBRIGHT, Endocrinology **20**:24 (Jan.) 1936.

In previous papers in this series evidence was given that the hypofunction of the ovary is primary and not secondary at the time of the menopause. Albright called attention to the usefulness of a quantitative determination of the ovarian hormone and the gonad-stimulating element of the anterior lobe of the pituitary. He concluded from his observations that the ovary is primarily at fault and that the gonad-stimulating hormone of the anterior lobe not only continues to be formed but is secreted in increased amounts. In the present contribution he cites data obtained from eleven patients with artificially or spontaneously induced menopause. The number of hot flashes per unit of time is plotted against the excretion of the estrogenic substance and the level of the follicle-stimulating factor of the anterior lobe of the pituitary in the urine. The effect of administration of the estrogenic substance and the withdrawal of this medication on these three variables was noted. He finds that there is adequate evidence of hypofunction of the ovaries as a primary deficiency and contends that the menopause is a physiologic "ovarian amenorrhea." The two most pronounced changes in the menopausal hormone pattern are underproduction of estrogenic substance and overproduction of the follicle-stimulating factor of the anterior lobe. Either of these abnormalities or a third might account for the vasomotor symptoms of the menopause. He calls attention to the long latent period between ovarian extirpation and the appearance of hot flashes. He also notes that the level of estrogenic substance during the menopause can be brought above normal with estrogenic therapy and may remain high for a long time before the hot flashes cease. He cites a third point, that lack of estrogenic substance due to disease of the pituitary is not accompanied by hot flashes. He found that estrogenic treatments stop the overproduction of the follicle-stimulating factor of the anterior lobe, and he intimates that the estrogenic substance may exert its beneficial effect by decreasing this factor. He implies that because the estrogenic substance exerts its beneficial effect at the menopause indirectly, the time element as well as the daily dosage is an important factor in the amount of improvement that occurs.

PALMER, Philadelphia.

CHRONIC HYPOGLYCEMIA. M. A. GOLDZIEHER, Endocrinology **20**:86 (Jan.) 1936.

Goldzieher reports 112 cases of chronic hypoglycemia in which a wide variety of somatic and emotional symptoms is presented. The blood sugar content of the patients during fasting varied from 53 to 111 mg. per hundred cubic centimeters, with an average of 80 mg. Sugar tolerance tests showed curves with the peaks at an average of 111.5 mg. After three hours the average height of the curves dropped to 72.5 mg., and at the fourth hour, to 64 mg. The most usual manifestations of chronic hypoglycemia were abdominal pain, excessive hunger or craving for carbohydrates, with resulting obesity, mild or severe fainting spells, tachycardia,

epileptiform seizures, speech defects and dysmenorrhea. Goldzieher found that 88 of the 112 patients showed signs of hypopituitarism, while 20 gave evidence of hypothyroidism. The condition of 74 patients was improved with organotherapy (anterior pituitary and thyroid extract) and dietary measures. Resection of the pancreas in one case failed to check the symptoms or influence the hypoglycemia for more than an initial period after operation. Goldzieher emphasizes his belief that hyperinsulinism is only rarely the result of hyperproduction of insulin alone and that the organic picture should be sought in the pituitary and thyroid glands.

PALMER, Philadelphia.

CACHEXIA HYPOPHYSIOPRIVA (SIMMOND'S DISEASE) WITH THYROID AND SUPRARENAL INSUFFICIENCY. E. ROSE and G. WEINSTEIN, Endocrinology **20**:149 (March) 1936.

Rose and Weinstein report a case of pituitary cachexia in a Syrian woman aged 44 whose symptoms began after a difficult labor at the age of 33 years. The patient had been seen three years before, and a diagnosis of myxedema was made. The terminal picture was that of high fever, azotemia, hypoglycemia and hemoconcentration. Pathologic observations included marked atrophy, fibrosis and destruction of the normal architecture of the anterior lobe of the pituitary, cortex of both the adrenal glands and the thyroid. The posterior lobe of the pituitary gland and the pancreas were not affected. Rose and Weinstein point out certain features of the case which may indicate that the immediate cause of death was failure of adrenal function.

PALMER, Philadelphia.

THE BIOLOGIC EFFECTS OF THYMECTOMY. N. H. EINHORN and L. G. ROWNTREE, Endocrinology **20**:342 (May) 1936.

Einhorn and Rowntree studied the biologic effects of thymectomy in white rats. They made observations of the accruing retardation in growth in succeeding generations. Thymectomy performed on young rats from 17 to 24 days of age produced no recognizable influence on their growth and development. However, in the offspring of thymectomized rats definite retardation in growth occurred, as reflected both in the curves for body weight and in the measurements of body length. This constant effect was observed only during the first six weeks of life of the offspring of thymectomized parents. Subsequent growth was normal. Sexual development was approximately normal. The average retardation in growth at its maximum was 36.9 per cent at 30 days of age. Retardation was most marked in the third generation. When the thymectomized rats were given daily injections of 1 cc. of thymus extract, the growth curves for the young rats coincided closely with those for the normal animals used as controls. Einhorn and Rowntree do not draw any final conclusions from these observations.

PALMER, Philadelphia.

A VASOVAGAL ATTACK. T. E. GUMPERT, Lancet **1**:85 (Jan. 11) 1936.

Gumpert had the good fortune to take an electrocardiogram of a patient during a fainting attack. Several years ago Lewis drew attention to slowing of the pulse and lowering of the blood pressure observed during an ordinary attack of pain. More recently he again stressed these features in association with vasovagal attacks and pointed out that most faints in the absence of postural causes and heart block are, in fact, vasovagal in origin. The slowing of the heart is due to increased vagal tone and is relieved by the injection of atropine, but the lowered blood pressure is an independent phenomenon and presumably is due to dilatation of the splanchnic vessels. The combination of these two factors is sufficient to rob the brain of an adequate supply of blood, with the result that consciousness is either completely or partially lost.

A man aged 46 gave a history of edema and ascites of a few months' duration. Gumpert had just removed a few cubic centimeters of blood from a vein at the elbow for a sedimentation test. At sight of the blood in the syringe, the patient became pale and sweated but did not lose consciousness. A few minutes later, while sitting in the electrocardiograph chair, he fainted. The pulse at the wrist could not be palpated. With a nurse supporting the patient, Gumpert obtained an electrocardiographic record of the vasovagal attack.

His findings indicate that the slowing of the heart was due to taking over by the auriculoventricular node of the function of the sino-auricular node as pacemaker. Separate leads showed that the impulse arose at different levels in the auriculoventricular node. On recovery sino-auricular rhythm, with its enhanced rate, was restored.

WATTS, Washington, D. C.

PATHOGENESIS AND HYPOPHYSIAL ORIGIN OF MARFAN'S SYNDROME. J. FRANÇOIS, Ann. d'ocul. **172**:700 (Aug.) 1935.

In a patient with Marfan's syndrome, with ectopia of the crystalline lens, François noted various endocrine symptoms which permit one to associate this disease with hypophysial dystrophy. The fundamental symptom was gigantism, which must be caused by hypersecretion of the hormone of growth by the eosinophilic cells. In addition to hyperfunction, there were other symptoms of insufficiency of secretion of the basophilic cells, the number or activity of which was diminished. These symptoms were: aplasia of the genital organs and absence of hair, decrease in the basal metabolic rate, reduction of the urea and urinary excretion, a generally slender exterior aspect, absence of cellulofatty tissue, lack of muscular development, hypotension, hypocholesteremia, hypoglycemia and increase in sugar tolerance.

François believes that in all cases Marfan's syndrome must be associated with hypophysial dystrophy. This disease is related to acromegaly and hypophysial gigantism. The differentiation of these three affections depends solely on the age at which the disease appears; e. g., Marfan's syndrome appears in the embryo, gigantism in the adolescent and acromegaly in the adult.

BERENS, New York.

EUNUCHS: AN ANATOMICOCLINICAL AND ANTHROPOLOGIC STUDY. MAZHAR OSMAN and IHSAN SCHUKRU, Hyg. ment. **30**:33 (Feb.) 1936.

A brief review of the history and frequency of eunuchs in Turkey is presented. With the establishment of the republic these persons were made citizens. When castration has occurred before puberty, the usual findings are a high thin voice; long, thin extremities; emaciated body; narrow shoulders; fat pads on the lower part of the abdomen and the hips; slender fingers; small face; occasionally some development of the breasts; slow, undulating gait, and shortness of breath. In personality they are polite, clean, childish, given to jealousy, users of cosmetics and jewelry, fond of titles and honors, loyal and timid. The phenomena of advancing age are slow in appearing. Sexual desire and orgasm are frequently present.

Three cases are reported in some detail, one with complete pathologic observations. All three patients had been deprived of all external genitalia. The first had a typical manic-depressive psychosis and during the attacks went through violent sexual activities. Death was due to tuberculosis. The second man had paranoia. The third suffered from melancholic and persecutory states and died of a cerebral accident at 60. In addition to the obvious changes in the brain associated with the vascular damage, there were hypertrophy of the anterior lobe of the pituitary gland, with increase of the eosinophils, lipoids and adenomatous tissue; atrophy of the thyroid; thin vocal cords, and increase in the interstitial tissue of the adrenal medulla.

ANDERSON, Los Angeles.

PROGRESSIVE LIPODYSTROPHY. H. ROGER, J. ALLIEZ and J. E. PAILLAS, Rev. franç. d'endocrinol. **13**:443 (Dec.) 1935.

Progressive lipodystrophy was known to the prehistoric cave-dweller, as Guiart has recently reproduced an ivory figurine with lipodystrophic features. Ameline and Quercy expressed the belief that Pharaoh Amenophis IV suffered from the same disease. Although credit must be given to Morgagni for drawing attention to this condition, the first accurate descriptions were made by Barraquer and Simons, by whose names the disease is now known. In addition to the classic features described by Simons, others have noted vasomotor disturbances, mental manifestations in the form of anxiety states, polyuria and glycosuria and bony deformities. The authors mention the anatomic changes, such as atrophy of the hypophysis, in the case of Zalla; ovarian lesions, in the case of Laignel-Lavastine; increase in the chromophilic and eosinophilic cells of the hypophysis, noted by Marburg, and slight increase in fat tissue and pigment cells of the adrenal cortex, in the case of Hussler. Comparing this condition with Cushing's syndrome, which presents the opposite picture, they suggest the possibility of opposite factors operating in the two entities. They realize, however, that this theory is highly speculative, since numerous experiments on the hypophysis failed to reproduce the condition and administration of pituitary gland preparations has not influenced the course of the disease.

They also consider the possibility of involvement of the central nervous system proper. In this connection they mention the theory advanced by Meige of a congenital or acquired defect in the segmental trophic centers of the spinal cord or in the sympathetic centers as an explanation of the metameric distribution of the atrophy. They see another possibility in the involvement of the metabolic regulatory centers in the diencephalon. They admit, however, that such a theory is not tenable.

They report a typical case of progressive lipodystrophy and believe that they were dealing with pronounced involvement of the autonomic-endocrine systems; they invoke the following points in favor of this possibility: Alteration in the vascular systems in their case is evidence of hypophysial dysfunction, as the same condition was present in the case of Long and Bickel, in which the pituitary showed definite changes. The disturbance in sugar metabolism is evidence of autonomic involvement, while the results of the interferometric tests speak in favor of widespread glandular dysfunction. They discuss the paradoxical association of chronic arthritis and pronounced hypotonia in their case and suggest that fatty atrophy, arthritis and hypotonia are probably all of the same origin. They believe that diencephalic involvement could explain the metabolic, arthritic and tonic disturbances, and in support of this assumption they invoke the striatal changes observed in the case of lipodystrophy of encephalitic origin reported by Sarbo.

NOTKIN, Poughkeepsie, N. Y.

FURTHER EXPERIMENTAL INVESTIGATION ON THE ENCEPHALIC CENTERS REGULATING VEGETATIVE FUNCTIONS. L. RICCITELLI, Riv. di pat. nerv. **45**:499 (May-June) 1935.

Riccitelli reports experiments in rabbits tending to prove that the diencephalon and the periventricular gray matter of the third and fourth ventricles play an important rôle in regulating some of the most important functions of metabolism including hematopoiesis. He found an increase in the number of blood platelets after experimental lesion of either the infundibular region or the fourth ventricle. In the same group of animals he observed an increase, and occasionally a decrease, in the number of red cells. In similar experiments he found that there are an increase in the sedimentation rate, an increase in the temperature of the animal's body and a tendency toward an increase of the alkali reserve. He found also that lesions of the diencephalon cause a decrease in the amplitude of oscillations in the electrocardiogram and that lesions of the fourth ventricle cause an increase.

FERRARO, New York.

Treatment, Neurosurgery

GENERAL PARESIS: TREATMENT BY TRYPARSAMIDE—INDUCED FEVER SEQUENCE. H. C. SOLOMON and S. H. EPSTEIN, Am. J. Syph., Gonor. & Ven. Dis. **20**:281 (May) 1936.

Fever and tryparsamide are the mainstays in the treatment for dementia paralytica. They may be used in four ways: tryparsamide alone, fever alone, tryparsamide followed by fever or fever followed by tryparsamide. From their own experience and a review of the literature, Solomon and Epstein compute the proportion of cases in which the disease was arrested by treatment as follows: with malaria alone, 25 per cent; with malaria followed by tryparsamide, 36 per cent; with tryparsamide alone, 42 per cent, and with tryparsamide followed by malaria, 85 per cent. The last figure was obtained from a study of twenty-one patients who had received treatment with tryparsamide without success. This refractory group of patients was submitted to fever therapy, with excellent results. Two patients received typhoid vaccine; one had both diathermy and malarial treatment, and the other eighteen received injections of the malarial organism. At the conclusion of this program all twenty-one of these patients were clinically and serologically better than they had been subsequent to the course of tryparsamide and prior to the fever regimen. All had had positive Wassermann reactions of the spinal fluid before the induction of fever; in only two was the fluid positive after pyretotherapy. The number of chills permitted each patient varied from eight to twenty-one. At the conclusion of treatment the condition of three patients was stationary; six were better but still had some defect, and twelve had improved clinically. Solomon and Epstein believe that an extended course of tryparsamide markedly enhances the chances of therapeutic effectiveness in a subsequently administered course of fever therapy.

DAVIDSON, Newark, N. J.

FATALITY FOLLOWING BISMARSEN THERAPY. J. H. SWARTZ, M. M. TOLMAN and HAROLD LEVINE, Arch. Dermat. & Syph. **33**:874 (May) 1936.

Although many other untoward effects of bismarsen therapy have been reported, no cases of fatal fat embolism following the use of this drug are known. The patient whose case is reported in the paper had received bismuth, neoarsphenamine, tryparsamide and bismarsen. He tolerated the first three drugs without difficulty but died within twenty-four hours after the third injection of bismarsen. The clinical manifestations of the preagonal collapse included fever, chills, sweats and jaundice. Autopsy disclosed a healed aneurysm in the wall of the heart, a small gallstone, aortitis with dilatation, hemorrhagic infarct of the spleen and fat emboli in the lungs and kidneys. Fatty changes in the liver were insignificant, and except for the bile-tinged cisternal fluid the central nervous system was normal. The fat emboli in the lungs and kidneys were revealed only by staining the tissues with scarlet red. They produced a "beaded" appearance within the alveolar walls and glomerular tufts, branching out in the conformation of capillaries and constituting intracapillary plugs of fat. The authors believe that the arsenical rather than the bismuth part of the drug is responsible for the toxic effect.

DAVIDSON, Newark, N. J.

RELATIVE VALUES OF CAFFEINE AND HYPERTONIC DEXTROSE AND SALINE SOLUTIONS IN REDUCING CEREBROSPINAL FLUID PRESSURE. ABRAM BLAU, Arch. Int. Med. **57**:749 (April) 1936.

A 15 per cent solution of sodium chloride lowers cerebrospinal fluid pressure more effectively than injections of a hypertonic solution of dextrose. The saline solution should be administered intravenously, and a dosage of 100 cc., injected slowly, is recommended. Five minutes or longer should be taken for this injection Blau compared the effect on manometric readings of the spinal fluid pressure of (1) a 50 per cent solution of dextrose, (2) a 15 per cent saline solution and (3)

5 grains (0.3 Gm.) of caffeine with sodium benzoate. In doses of 50 cc. the dextrose lowered the pressure in only two of fifteen cases; in doses of 100 cc. a reduction was effected in only five of thirteen cases. In some instances the intravenous injection of a hypertonic solution of dextrose actually raised the pressure. Caffeine lowered the cerebrospinal tension, but its effect was temporary. The intravenous injection of a 15 per cent saline solution, on the other hand, was always followed by a prolonged reduction in cerebrospinal pressure. The toxic effects of the saline solution were negligible, and Blau recommends its use instead of dextrose as a routine whenever a reduction in cerebrospinal fluid pressure is desired.

DAVIDSON, Newark, N. J.

ESSENTIAL HYPERHIDROSIS CURED BY SYMPATHETIC GANGLIONECTOMY AND TRUNK RESECTION. ALFRED W. ADSON, WINCHELL CRAIG and GEORGE E. BROWN, Arch. Surg. **31**:794 (Nov.) 1935.

Essential hyperhidrosis affecting the hands and feet is frequently a disabling disease and seriously interferes with the patient's ability to earn a livelihood. Observations indicate that the severity of the condition and the areas involved by the excessive sweating are controlled by cerebral influence. Complete cure is effected by sympathetic ganglionectomy.

GRANT, Philadelphia.

INTRASPINAL INJECTION OF ALCOHOL FOR INTRACTABLE PAIN. W. RITCHIE RUSSELL, Lancet **1**:595 (March 14) 1936.

In 1930 Dogliotti introduced the intraspinal injection of alcohol as treatment for relief of intractable pain. Dogliotti obtained good results in a large proportion of cases, and satisfactory effects have been reported by others. Russell has used this procedure in twenty-two cases, most of which were instances of inoperable malignant disease associated with severe pain that was not relieved by opiates. In order to relieve pelvic pain or other pain conducted through the sacral nerves, the sacrum must form the highest part of the spinal canal during and for a period following the injection. The patient lies in the usual position for a lumbar puncture. The side of the body on which there is pain is uppermost. Pillows are placed under the hips to raise the sacrum. From 0.4 to 0.8 cc. of absolute alcohol is injected slowly, the alcohol rising to the uppermost part of the spinal canal. The patient is required to lie in this position for one hour, so that the alcohol will not diffuse and will remain in contact with the proper posterior roots. In cases of an advanced stage of carcinoma which is not relieved by small amounts of alcohol, larger amounts have been used. Complications such as retention of urine and weakness of a lower extremity are the most frequent. To obtain relief from pain in other parts of the body, the patient's position should be such as to place the affected region uppermost.

Relief of pain was obtained in fourteen cases, partial relief in three and none in five. Incontinence of urine followed the injection in one case, retention of urine in two and transient weakness of one leg in three. It is Russell's opinion that at present the treatment should be used only in cases of advanced inoperable malignant disease.

WATTS, Washington, D. C.

TREATMENT FOR SCHIZOPHRENIA WITH PLACENTAL BLOOD. J. S. GALANT, Monatschr. f. Psychiat. u. Neurol. **90**:265 (Feb.) 1935.

Intramuscular injections of placental blood were given to forty-one patients with schizophrenia, twenty-five of whom had the catatonic form of the disorder. In twenty-six patients the illness was of short duration, and in fifteen there had been long-standing mental symptoms. In the former group seven patients had complete remission, and fourteen showed definite improvement; in the latter group one patient had a remission, and six exhibited improvement. As a rule fifteen injections of from 4 to 10 cc. were administered to each patient. The treatment

is not dangerous. Rise of temperature can usually be avoided if the placental blood is used on the day on which it is obtained. According to Galant, this type of treatment represents one of the better forms of active therapy for schizophrenia. It leads to improvement of the physical condition of the patient, with considerable gain in weight. Stuporous patients become more active, and excited patients become quieter. The efficacy of placental blood may be due to its hormonal or its protein content or to both factors. The treatment has an additional indirect psychotherapeutic effect, which is attributed to emotional and suggestive influences.

ROTHSCHILD, Foxborough, Mass.

A NEW TREATMENT FOR CEREBRAL HEMORRHAGE AND ITS SEQUELAE. ROSOLINO COLELLA and GIUSEPPE PIZZILLO, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:337 (March) 1935.

Colella and Pizzillo report the results of treatment for intracranial hemorrhage with autohemotherapy. Thirty-five cases were studied. No percentages of favorable outcome are given. From 20 to 30 cc. of blood is taken from the vein of the arm or foot and injected immediately into the muscles of the gluteal region of the unaffected side. To prevent clotting a few cubic centimeters of a 25 per cent solution of sodium citrate solution is drawn into the syringe before the blood is taken from the vein. Eight cases are reported in some detail. Striking improvement in consciousness and motor power was observed immediately after the injections. Without knowing the precise mechanism, the authors claim that these intramuscular injections of the patient's own blood stopped the intracranial bleeding and in some unknown way also stimulated the recovery of function of the affected neural tissue. This method is of value in treatment of all forms of intracranial hemorrhage, regardless of the age of the patient or the etiology. Especially favorable results were noted in cases of head injury. The method is of more value if used immediately after the injury. The authors suggest also its prophylactic use in hypertensive patients who show prodromal symptoms of an imminent cerebral accident. The injection of blood aids in the differential diagnosis between softenings due to vascular occlusions and hemorrhage. No similar, favorable results have been noted in instances of cerebral infarct.

SAVITSKY, New York.

Special Senses

BILATERAL RETROBULBAR OPTIC NEURITIS FOLLOWING INTRAVENOUS INJECTION OF ALCOHOL DURING THE COURSE OF A PUERPERAL INFECTION. V. MORAX, Ann. d'ocul. **172**:301 (April) 1935.

Morax reports the case of a woman aged 25 who appeared to be in perfect health and in whom there developed serious puerperal infection after the delivery of a stillborn child. Treatment with various serums was unavailing. On the eighteenth day she received an intravenous injection of 200 cc. of 33 per cent alcohol, which was followed by gastric and visual disturbances. After six weeks her health improved, but at the time of writing she believed that vision was decreasing and that she would lose her sight completely.

Ocular examination revealed that the patient had a good sense of direction and was able to avoid all obstacles. Nevertheless, in spite of normal refraction, central visual acuity was lowered (she counted fingers at 2 meters). The reflexes to light and the media were normal. Pallor of the disks was equal on the two sides. Perimetric examination showed the presence of an absolute central scotoma of from 10 to 15 degrees on each side, but the scotoma extended to the right as well as to the left of the nasal side. The tension was normal.

Morax believes there are several objections to the hypothesis of an alcoholic toxic neuritis. Alcoholic retrobulbar neuritis usually occurs in cases of chronic intoxication with alcohol and nicotine. In this case the supposed alcoholic intoxication developed rapidly after injection of alcohol into the veins. Acute intoxication

with ethyl alcohol does not furnish a basis for retrobulbar neuritis. This statement does not hold true for methyl alcohol (wood alcohol), which has sometimes been substituted for ethyl alcohol in preparing liquors of low quality and some pharmaceutic products. If the alcohol used for the intravenous injection had been adulterated by the addition of methyl alcohol, this would explain all the symptoms, including the gastric and visual disturbances. However, Morax does not make this conclusion definite.

BERENS, New York.

OPTIC NEURITIS OCCURRING DURING TREATMENT WITH INJECTIONS OF PENTAVALENT ARSENIC. P. VEIL, Ann. d'ocul. **172**:314 (April) 1935.

Veil reports the case of a patient with tabes who received injections of acetylarsan (the p-oxyacetylaminophenylarsinate of diethylamine). The result was total blindness of one eye and partial atrophy of the optic nerve of the other, without central scotoma. Veil also reports a case of unilateral optic neuritis, which occurred during treatment with injection of arsaminol (a Japanese preparation of arsphenamine). In this case neuritis without central scotoma was cured by injections of sodium thiosulfate. In this patient Ambard's constant was high.

BERENS, New York.

TWO CASES OF BLINDNESS CAUSED BY TREATMENT WITH ACETARSONE IN PATIENTS WITH DEMENTIA PARALYTICA. SALGO, Ann. d'ocul. **172**:314 (April) 1935.

Salgo reports two cases of blindness caused by bilateral retrobulbar optic neuritis in a series of one hundred and twenty patients with dementia paralytica who were treated by sodium acetarsone. Since it is often impossible to make examination for contraction of the visual field, central scotoma or other signs of optic neuritis in cases of this kind, it is necessary to test the visual acuity before each injection.

BERENS, New York.

HEARING IN SENSORY APHASIA. FERDINAND MOREL, Encéphale **30**:533, 1935.

The last segment of the auditory pathway, extending from the medial geniculate body to the cerebral cortex, is of special importance because its destruction can result in aphasic disturbances. The rarity of deafness, either ipsilateral or crossed, following lesions of the terminal segment of the auditory pathway, shows that the decussation is not total. In dogs conditioned to respond to a tone of 1,000 vibrations, the auditory cortex of both hemispheres must be removed before a marked reduction of auditory acuity takes place. There is no difference between the right and the left hemisphere with respect to auditory acuity.

Six cases have been reported of total unilateral destruction of the auditory radiations in which the patient's hearing was studied. In five cases the left side was involved and in one the right. In no case was auditory acuity diminished. Morel adds the case of a patient aged 50 years who had signs of total softening of the superficial territory of the left middle cerebral artery, beyond the origin of the ascending branches. The transverse temporal gyrus was undoubtedly involved. The audiogram was normal and equal for the two sides. On the basis of the conservation of hearing after total right hemispherectomy Dandy concluded that there is no acoustic center in the right temporal lobe. Morel, however, concludes from the same data that the two temporal lobes are equipotential so far as elementary hearing is concerned.

Bilateral lesions of the terminal segment of the auditory path result only in diminution or abolition of hearing. When this central deafness is complete, it is indistinguishable from bilateral labyrinthine deafness as regards elementary hearing. The transverse temporal gyrus is necessary for elementary hearing, while the first, second and third temporal gyri are not.

The equipotentiality of the right and left temporal lobes disappears when one goes beyond elementary hearing to the recognition, identification and understanding

of sound complexes, abolition of which constitutes auditory agnosia. Global auditory agnosia, involving recognition of music, noises and words, results from section of the auditory radiations at or near their junction with the cortex of the transverse temporal gyrus. Section of the radiations farther from the cortex does not produce agnosia. These two facts suggest that the callosal fibers from the right temporal lobe join the left radiations just before reaching the projection area. The integrity of the former would be sufficient to prevent agnosia. Dissociated agnosias appear when the radiations and the projection area themselves are spared, while circumscribed areas of the left temporal lobe are destroyed. Thus, destruction of the left temporal pole results in musical agnosia and that of the posterior part of the first temporal gyrus in relatively pure word deafness. Agnosia for sounds, sometimes called mind deafness, is always associated with verbal or musical agnosia or both. Word deafness itself seems to be dissociated into many lesser deficiencies, the localizations of which form, according to Bárány, a "scale" between the projection area and the zone of Wernicke. The complexity of this grouping is "astronomic," and one can at best hope to describe only its "crude resultants." Thus, to different word-deaf patients words appear as a murmur, as a rustling of wind among leaves, as speech impaired by poor acoustics or too great a distance of the speaker or, lastly, as a foreign language. The limit between paracousis and paragnosis is difficult to trace.

In progressive symmetrical temporal atrophy (Pick's disease), verbal agnosia appears first and gradually becomes cortical deafness. This corresponds to the anatomic course of the disease, the transverse temporal gyrus being the last to atrophy.

LIBER, New York.

Experimental Pathology

EPIDEMIOLOGY OF EQUINE ENCEPHALOMYELITIS IN THE EASTERN UNITED STATES. C. TENBROECK, E. W. HURST and E. TRAUB, J. Exper. Med. **62**:677, 1935.

Equine encephalomyelitis of the eastern type is a disease of the late summer and fall, and cases are found in greatest numbers near salt marshes. The epidemiologic findings are against its transmission by contact and favor the view that it is insect borne. Although virus can be demonstrated in the blood of infected horses, it is present for a relatively short time, and the possibility that the disease is not primarily an infection of horses but is transmitted to them from another host is considered.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

A STUDY OF THE ACTION OF BROMIDES IN CLINICAL AND EXPERIMENTAL EPILEPSY. BENJAMIN BOSHES, J. Nerv. & Ment. Dis. **83**:390 (April) 1936.

Study of patients with epilepsy indicates that they may be divided into three groups, according to their response to bromides: (1) those in whom seizures are completely prevented, 43 per cent; (2) those in whom grand mal seizures persist, 26.4 per cent, and (3) those in whom petit mal seizures persist, 30.6 per cent. Patients in whom petit mal seizures persisted were given a larger oral dose and attained a higher level of bromides in the blood, while those in whom seizures could be prevented required as a group a lower oral intake of bromides and presented a lower level of bromides in the blood. Bromide intoxication was seen in the three groups but occurred most frequently in patients with grand mal seizures. A high level of bromides in the blood with a relatively low oral dosage indicates a tendency to store bromides, and though the explanation is not complete, there seems to be a renal and gastro-intestinal factor. It is established that constipation predisposes to bromism. Pollock found that bromism developed only in 15 per cent of patients, when constipation was avoided.

Attempts to produce seizures in bromide-fed rabbits with a standard 2 per cent emulsion of thujone in 6 per cent acacia were unsuccessful, since high levels of bromide in the blood tend to ameliorate or completely prevent the induced seizures.

An attempt to explain the action of bromides by assuming an alteration of the total halide content of the blood was not substantiated in the studies on animals. Bromides replace chlorides, ion for ion, and vice versa. In bromized rabbits the bromide concentration of the brain is very slight, particularly in cases in which the animal has been exsanguinated, and it bears no constant relationship to the bromide level of the blood.

A hypochloremic state does not prevent seizures in rabbits induced with thujone. The anticonvulsant effect of bromides is due to the action of bromide ions and not to the deprivation of chlorides.

HART, Greenwich, Conn.

HISTOLOGIC SUBSTRATUM OF EXPERIMENTAL EPILEPTIC SEIZURES INDUCED WITH ABSINTHE (ARCHITECTURAL CHANGES IN EPILEPSY). A. D. SURABASCHWILI, Monatschr. f. Psychiat. u. Neurol. **90**:221 (Jan.) 1935.

Epileptic attacks were produced in four dogs by the injection of absinthe and in one dog by electrical stimulation of the brain. Examination of the brains of these animals disclosed acute degenerative changes of the nerve cells of the cerebral cortex. The second, third and fifth cortical layers were chiefly affected. The severest involvement occurred in the frontal lobe, with the motor area presenting the greatest alterations. The temporal lobe was damaged to a less extent, but parts of Sommer's sector of the cornu ammonis were severely involved. Outspoken abnormalities were not observed in other parts of the brain. Surabaschwili concludes that absinthe is a cortical poison and looks on the changes in the frontal and temporal lobes as the morphologic substratum of the convulsions produced by its administration to dogs. He is of the opinion that any part of the nervous system may serve as the point of origin of epileptic attacks. However, in higher animals, as well as in man, it appears that complicated activity of the whole nervous system with active participation of the cerebral cortex is necessary for the development of typical convulsive seizures.

ROTHSCHILD, Foxborough, Mass.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, Nov. 10, 1936

THOMAS K. DAVIS, M.D.

President of the New York Neurological Society, Presiding

CALCIFIED SUBPIAL LESION OF THE SPINAL CORD, WITH VARICOSE VEINS. DR. CLARENCE C. HARE and (by invitation) DR. WILLIAM H. EVERTS.

A white man aged 39 was admitted to the Neurological Institute of New York because of weakness and numbness of both legs. About twenty-one years before, he fell from the back of a truck, landing on his abdomen. He experienced no symptoms as a result of this and went about his usual duties. Six months later he felt a dull, throbbing pain in the lumbar region of the spine, which radiated around the trunk at the level of the lower costal margin. Several months later, while he was at work, the pain became such that he had to lie down; on arising four hours later the right leg felt weak and the left leg numb. There was gradual improvement in this condition during the following year; he was able to return to work and continued until the summer of 1935. At this time both legs felt weak, and the right leg appeared to be atrophied. In February 1936, after a lumbar puncture, his legs became so spastic and weak that he could hardly walk.

Examination disclosed spastic paraplegia, with increase of tendon reflexes in the lower extremities and the Babinski toe sign bilaterally. The muscles of the right leg and thigh were atrophied, and there were fibrillations in the muscles of both thighs. Sensibility to pain and touch was diminished in both legs and increased over the lower thoracic segments. A sensory level was present at the ninth thoracic dermatome. The pilocarpine sweating test revealed a level at the tenth thoracic segment. Manometric studies showed no block.

Roentgenograms of the spine showed calcification in the spinal canal opposite the eleventh and twelfth thoracic vertebrae, measuring 5.5 cm. in length and 2 cm. in width. All laboratory studies gave normal results except that the reaction of the spinal fluid to the globulin test was 1 + and there was 46 mg. of protein per hundred cubic centimeters of spinal fluid.

Laminectomy was performed on the tenth, eleventh and twelfth thoracic vertebrae. A mass of varicose veins was exposed beneath the dura, at the superior portion of the incision. The spinal cord opposite the eleventh and twelfth thoracic vertebrae appeared to be entirely calcified. Palpation with forceps revealed that the cord was as hard as bone; the calcification was definitely intramedullary.

The postoperative course was uneventful. There was slight improvement in the ability to walk; the sensory level receded several segments.

It was concluded that this patient had had a slow hemorrhage beneath the pia-arachnoid some months after the trauma and that the hemorrhagic area had calcified slowly and produced the symptoms. The varicose veins were considered to be the result of impeded circulation.

This article will appear in full in the *Bulletin of the Neurological Institute of New York* (June 1937).

DISCUSSION

DR. RICHARD BRICKNER: Does not Dr. Hare think it is equally possible that the varices were present before the injury and that this was the reason for the peculiar type of hemorrhage?

DR. ISRAEL S. WECHSLER: The patient was in my service before transfer to the surgical division. A tentative diagnosis of compression and afterward of tumor was made from the roentgenograms. My associates and I were unable to correlate the injury with the present condition. The normal results with the manometric test caused further doubts, while the roentgen findings came as a complete surprise. The presence of varices was unsuspected. I have never seen a similar case and did not think of calcification of the meninges.

DR. HERMAN SELINSKY: In postmortem examination in cases in which there are no neurologic signs, one not infrequently observes plaques lying on the spinal cord, with a few varices. These are considered to be without significance. In this case one sees an exaggerated form of such calcification, with marked varices. Has Dr. Hare any idea why these conditions occur in the spinal cord? They are extremely uncommon in the pia-arachnoid over the brain.

DR. CLARENCE C. HARE: In answer to Dr. Brickner: It is possible that the varices may have been present before the calcified area developed. This seems unlikely, however, in view of the fact that this man had no symptoms prior to the trauma. Would it not be better to assume that he had no abnormalities prior to that time?

In response to Dr. Selinsky: I have no idea what relation the calcification in this case has to the type observed in postmortem examinations made as a routine. One commonly sees small calcified areas in roentgen films of the vertebral column made as a routine in patients presenting no neurologic signs of involvement of the spinal cord. It is surprising that this man was able to do as much as he did, in view of the apparently complete calcification of this portion of the spinal cord.

RELATION BETWEEN FUNCTION AND VASCULARITY IN THE NERVOUS SYSTEM. DR. HENRY S. DUNNING (by invitation) and DR. HAROLD G. WOLFF.

The arrangement of neurons is such that cell bodies are grouped together in masses denominated centrally as gray matter and peripherally as ganglia, whereas axons are grouped together in bundles called centrally white matter and peripherally nerves. Masses of cell bodies may be separated into two groups: 1. The gray matter and the ganglia of the autonomic nervous system, which contain cell bodies with dendrites in synaptic connection with the terminal arborizations of axons. This combination of dendrites and axonal arborizations is known as the neuropil and is the structural basis of the synapse and of integrative function.

2. The dorsal root ganglia of the spinal nerves and the analogous structures of the cranial nerves, which contain cell bodies that are unique in the lack of processes structurally definable as dendrites and of synaptic connections with the arborizations of axons. Therefore, portions of the nervous system may be isolated for study consisting of a common stroma of interstitial cells and blood vessels, together with different components of the neural parenchyma, a natural separation occurring as follows: (1) nerve cell bodies and axons with synaptic structures; (2) nerve cell bodies and axons without synaptic structures, and (3) axons alone.

Craigie, who determined quantitatively the relative vascularity of various parts of the central nervous system of the albino rat (*J. Comp. Neurol.* **31**:429, 1919-1920), observed that the gray matter is more vascular than the white matter and can be divided into two distinct groups: the motor nuclei and the correlation nuclei, the latter, of which the dorsal cochlear nucleus ranks first, being more richly supplied with blood vessels. Craigie stated that although there is no proof that such a difference in vascularity necessarily implies a corresponding difference in metabolic activity in the regions concerned, this assumption seems to be the only reasonable explanation of the facts and is in accord with what is known of the blood supply of other tissues.

There is evidence of a quantitative relation between vascularity and oxygen consumption in the more recently published data of E. G. Holmes on the oxygen consumption in vitro of various parts of the nervous system of mammals. He

found that the oxygen consumption of the cerebral cortex is much greater than that of the white matter and of the nerves (*Biochem. J.* **24**:914, 1930) and that the consumption of the trigeminal ganglion "is of a very low order, much the same, in fact, as that of the peripheral nerve of the same animal." Because there are no dendrites or synapses in the trigeminal ganglion, he suggested that "oxidation and glycolysis in brain occur in the dendrites and synaptic structures rather than in the cell bodies" (*Biochem. J.* **26**:2005, 1932).

In order to prove or disprove the existence of a quantitative relation between vascularity and oxygen consumption in the nervous system, the vascularity of the parietal cortex, the superior cervical sympathetic ganglion, the trigeminal ganglion, the parietal white matter and the trigeminal nerve was determined quantitatively in the cat.

The method employed was: Into the blood vessels of these structures in 21 mature cats, under barbital narcosis, was injected a solution of berlin blue by various methods. Satisfactory injections were made in only 6 cats. The method used in all 6 animals consisted of the injection of from 190 to 300 cc. of the dye, at a pressure of from 10 to 12 ½ feet (305 to 380 cm.) of water, into the left common carotid artery. The structures on the side of the injection, after fixation in situ in a dilute solution of formaldehyde U.S.P. (1:10), were embedded in pyroxylin, and sections were cut at 20 microns. The length of blood vessels less than 20 microns in diameter was computed in millimeters per cubic millimeter of tissue, by means of an ocular micrometer. In each structure the blood vessels in the three most vascular areas in each of five sections were measured and averaged.

In all 6 cats the vascularity of each structure was consistently different, the average length of the blood vessels, expressed in millimeters per cubic millimeter of tissue, being: parietal cortex, 871 mm.; cervical sympathetic ganglion, 737 mm.; trigeminal ganglion, 513 mm.; trigeminal nerve, 412 mm, and parietal white matter, 374 mm. These results not only demonstrate that the vascularity of the cerebral cortex, the trigeminal ganglion, the trigeminal nerve and the white matter is roughly proportional to the oxygen consumption of these tissues in vitro, as determined by E. G. Holmes, but suggest that the presence of synaptic structures in the cortex and the sympathetic ganglion is causally related to the increased vascularity of these tissues over that of the trigeminal ganglion.

However, to prove that there is a quantitative relation between synaptic structures and vascularity it is necessary to demonstrate that there is a correspondence between the number of synaptic connections and the degree of vascularity and that there is no quantitative relation between vascularity and the other components of the neural parenchyma. That there is such a correspondence is suggested by the correlation of the results of two hitherto unrelated anatomic investigations. The first is that of Craigie (*J. Comp. Neurol.* **33**:193, 1921), who determined quantitatively the vascularity of the cell laminations in various areas of the cerebral cortex of the albino rat. He observed that in all areas lamina 4 (Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, Leipzig, J. A. Barth, 1909) is more vascular than any other layer, reaching a peak in the parietal area, where it ranks as the second most vascular part of the central nervous system. The second, and more recent, work is that of Poljak (*J. Comp. Neurol.* **44**:197, 1927). He produced an extensive lesion of one cerebral hemisphere in a cat, which involved the following parts (Campbell, A. W.: Histological Studies on the Localization of Cerebral Function, Cambridge, Cambridge University Press, 1905): precrucial or motor area, postcrucial or sensory area, ectosylvian areas A and B, extrarhinic area and optic radiations from the lateral geniculate body. After degeneration was complete, he studied the intact occipital cortex, where he observed the greatest amount of degeneration of myelin about the cell bodies in lamina 4. In consideration of the great extent of the lesion, which included not only the cortex but the white matter of the hemisphere, this experiment suggests strongly that synaptic connections are more numerous in the fourth layer than in any other lamina of the occipital cortex. Lamina 4 was also the most vascular layer of the parietal cortex in the one cat of this series in which the vascularity of the

laminations was determined. It is significant that lamina 1, in which there are relatively few nerve cell bodies from which extend numerous dendrites having synaptic connections (Ramón y Cajal, S.: *Trav. du lab. de recherches biol. de l'Univ. de Madrid* **19**:113, 1921), is relatively rich in blood vessels.

A correspondence between the number of synaptic connections and the degree of vascularity having been pointed out, before one concludes that synaptic structures are responsible for the increased vascularity of the cerebral cortex and the sympathetic ganglion over that of the trigeminal ganglion, it remains to be shown that there is no quantitative relation between vascularity and the other components of the neural parenchyma, that is, nerve cell bodies and axons. Because the vascularity of the white matter and the nerve is consistently less than that of the trigeminal ganglion, it is obvious that axons are not responsible for the increased vascularity of the cerebral cortex and the sympathetic ganglion. Therefore, to determine whether there is a correspondence between quantitative differences in the nerve cell bodies and the degree of vascularity, the number of cell bodies, the amount of substance of the cell bodies (in terms of the total area occupied by the cell bodies) and the vascularity were measured in laminae 1 and 4 of the parietal cortex and in the cervical sympathetic and trigeminal ganglia of one cat. All these measurements were made in the same sections of tissue, cut at 20 microns and stained by Nissl's method.

Tissue	Vascularity, Mm. per Cu. Mm.	No. of Nerve Cell Bodies per Sq. Mm.	Total Cross-Sectional Area of Nerve Cell Bodies, Sq. Mm. per Sq. Mm.	Average Cross-Sectional Area of Single Nerve Cell Bodies, Sq. Microns
Lamina 4	882	1,826	0.30	160
Cervical sympathetic ganglion	799	610	0.36	600
Lamina 1	733	334	0.03	90
Trigeminal ganglion	547	452	0.62	1,400

It will be seen that in lamina 1, where the number of cell bodies is least, the vascularity is more nearly maximal than minimal and that in the trigeminal ganglion, where the total cross-sectional area of the cell bodies is greatest, the vascularity is least. These results, therefore, indicate that there is no correspondence between the degree of vascularity and the number or mass of nerve cell bodies.

Conclusions.—The results of this work indicate that in the nervous system there are: (1) a quantitative relation between oxygen consumption and vascularity, (2) a quantitative relation between synaptic connections and vascularity and, since the integration of nerve impulses is the function of synaptic structures of neuropils, (3) a quantitative relation between integrative function and vascularity.

DISCUSSION

DR. HAROLD G. WOLFF: Every now and then, one needs reorientation in considerations of the nervous system. With improvement in histologic technic, the cell body and its axon have been beautifully visualized, and hence for a long time one has been accustomed to think in terms of these structures, which can be so readily studied. One looks for evidence of disturbance in function or of disease. If the results presented this evening are correct (and I think they are), one must remember that the part of this mechanism utilizing the most energy is not the most readily visible. The greatest metabolic activity occurs in the terminations of the axon and the dendrites. Now, it is conceivable that disease may seriously interfere with what is going on at the synapse without any histologically visible change occurring in the cell body, even though the staining technic is almost perfect.

The experiments of Kibjakow (*Arch. f. d. ges. Physiol.* **232**:432, 1933) on the cervical sympathetic ganglion may be relevant to this discussion, since this is a

structure with synapses about which much is known. The cervical sympathetic ganglion was perfused artificially, and it was observed that when the preganglionic fiber was stimulated, there appeared in the perfusate a chemical substance resembling acetylcholine. This material is produced in or about the synapses. The material resembling acetylcholine was liberated, and it is reasonable to infer that when energy is shifted from one form to another, energy is necessary to make the shift. Hence, at this site of liberation of the neurohumoral agent the greatest amount of blood would be necessary, and metabolism would be highest. This is in keeping with our results, which indicate that the blood supply at the synapse is greater than elsewhere in the nervous system. It is to be remembered, moreover, that the total neural surface area of the fine fibers of the neuropil is very great. This in itself may account for the greater metabolic activity.

It is known from the experiments of Gerard and Serota that if needle electrodes or a thermopile is placed in the occipital cortex and a light is flashed on the retina of a monkey, there is, shortly after the light has been flashed into the eye, a relative increase in heat production in the occipital cortex. This has been interpreted as due to vasodilation in the occipital lobe resulting from increased function brought about by the light flashing on the retina. It is probable that the inference is correct and that in the neuropils of the occipital cortex there is the basis for the increased metabolism incidental to increased function.

It seems that the cell body has long held a prominent place in considerations and that now one must turn again to more nebulous structures, hardly visible and almost conceptual—the synapses.

DR. S. BERNARD WORTIS: This is an excellent paper and is helpful in elucidating the concept of cortical circulation and its relation to cortical function. There are other aspects of the problem which appear to be of equal importance. Other substances which exist in the brain tissue must also be considered in evaluating the circulation of the brain or synaptic processes and their integrative function. Undoubtedly, these synapses and their functions are important, but should not one also consider the vitamin content, the enzymatic content and the chemical content of brain tissue in evaluating these data? For example, the work of Gerard, Sinclair and Peters has shown that vitamin B_1 is an important brain substance. A nervous system depleted of vitamin B_1 has a lower oxygenation rate than a nervous system possessing vitamin B_1 in adequate quantity; furthermore, if vitamin B_1 is given to the vitamin-deficient organism, the oxygenation rate of that nerve tissue will return to normal. Again it has recently been shown that vitamin C is similarly related to nerve function. As yet, little is known about the enzymatic functions of the brain tissue.

These data must also be related to the picture which Dunning and Wolff have shown. May one not pose the question in this way? Is one justified in assuming that the synaptic function alone is related to vascularity of the brain, without some knowledge of other factors, such as the focal distribution of the enzymatic content, the chemical nature and the vitamin content of the brain tissue?

Also, I wish to ask if the essayists have any idea concerning the vascularity of the brain as compared with the vascularity of the spinal cord in correlation with the so-called integrative function of these structures?

DR. LAWRENCE S. KUBIE: The conclusion of this interesting study is that the vascularity of different regions of the central nervous system depends on the amount of synaptic structure present per unit of mass. This conclusion is reached by inference from the fact that the degree of vascularity did not run parallel either to the number of nerve cell bodies or to the total area of nerve cells present in a typical section.

Approaching the subject critically, the simplest question is whether there is not a still more fundamental relationship between the amount of vascularity and the proportion of nerve elements, as opposed to relatively inert supporting tissues, in each unit of mass. Presumably, one purpose that the authors had in mind in counting the cells and measuring their areas was to test this question, their implicit assumption being that in sections in which nerve cells were more numerous

or larger in cross-section, the supporting tissues would be correspondingly less in total bulk. Whether this is a safe premise is hard to say; it is perhaps fair to ask them to discuss more fully this first assumption.

Presumably, the other purpose behind the counting of nerve cells and the measuring of their areas was to determine whether the vascularity of a unit of tissue runs parallel to its metabolic requirements. Here the tacit assumption was that the number of cells and their areas give an index of total metabolic activity. Again, one must make sure that this assumption is valid. In most physical systems the energy requirements depend not only on the total mass of the material or the cross-section or the number of units but on the minuteness with which the mass is subdivided, that is, on the total surface area in relation to the total mass. One would expect, therefore, that the energy requirements of nerve cells would have some relationship to the surface area, rather than to the number or size alone. Probably an approximate estimation of surface areas could be reached by a calculation based on the relationship of the total number of cells to average cell areas.

Without going through such a calculation, it is hard to say whether this would make any difference in the authors' conclusion; but it seems to me worth while to raise the point, for the same considerations arise with regard to current studies of the oxygen consumption of different types of nerve tissues.

DR. HENRY S. DUNNING: I shall ask Dr. Wolff to answer Dr. Wortis' question about the vitamins.

Concerning the relation between the vascularity of structures in the brain and that in the spinal cord Craigie has data. He found that in the albino rat the vascularity of the white matter of the cord is relatively low and that of the ventral gray matter considerably higher and that the dorsal gray matter, concerned with correlative function, is the most vascular portion of the cord. Although the vascularity of the dorsal gray matter of the cord is greater than that in some laminations of the cerebral cortex, the parts of the central nervous system richest in blood vessels are present in the brain, the dorsal cochlear nucleus ranking first and the fourth layer of the parietal cortex second.

In answer to the questions raised by Dr. Kubie: It might be well to consider the logical processes on which we have based our conclusion that there is a quantitative relation between synaptic structures and vascularity. Since tissue containing nerve cell bodies and axons with synaptic structures was observed to be more vascular than tissue containing nerve cell bodies and axons without synaptic structures, it was postulated that synaptic structures, that is, axonal arborizations and the dendrites intervening between the nerve cell bodies, may be responsible for the increased vascularity. This postulation was further substantiated by the correlation of the work of Craigie and Poljak, indicating that the degree of vascularity varies with the number of synapses. However, if it is true that synaptic structures are causally related to increased vascularity, it must be shown that the other components of the neural parenchyma, that is, nerve cell bodies and axons, are not so related. Because the vascularity of the white matter and the nerve is less than that of the trigeminal ganglion, it is obvious that axons are not responsible for the increased vascularity of the cerebral cortex and sympathetic ganglion. It remained to determine whether there is a correspondence between the degree of vascularity and quantitative differences in the nerve cell bodies. It was to answer this question that we counted the nerve cell bodies and measured the area occupied by them in the sections of known vascularity. The results indicate that there is no correspondence between the degree of vascularity and quantitative differences in the nerve cell bodies. Therefore, the conclusion that there is a quantitative relation between synaptic structures and vascularity is based not only on direct but on indirect evidence, secured by excluding from this relation the other components of the neural parenchyma. It has been assumed that the nonparenchymatous or supporting tissue, known to be qualitatively the same in all the structures compared, has a nutritional requirement similar to that of meningeal tissue, the oxygen consumption of which

Dr. Wortis has found to be about one-tenth that of brain tissue (*Am. J. Psychiat.* **93**:87, 1936). Hence, quantitative variations in the supporting tissue would not vitiate the conclusions derived from this comparison.

In studying quantitative differences in the nerve cell bodies in sections of nerve tissue, the usual procedure is to count the cell bodies within a given area. However, the number of cell bodies is not always an index of the amount of cell body substance in the tissue. For example, in the trigeminal ganglion, where the cell bodies are large and close together, relatively few cell bodies occupy twice as much space in the tissue as do four times as many in lamina 4 of the parietal cortex, in which the cell bodies are smaller and farther apart. Therefore, in a given area of tissue we not only counted the nerve cell bodies but measured the total area occupied by them, the latter measurement being considered an accurate index of the amount of cell body substance in the tissue. We have not calculated surface areas from these data, since it is evident that all the nerve cell bodies concerned in this study are not spherical.

Dr. Harold G. Wolff: Our data, that the ratio of the vascularity of the cortex to that of the trigeminal ganglion is 9:5, and data obtained by Dr. Wortis that the ratio of the oxygen consumption of the cortex to the oxygen consumption of the white matter is 3:1 or 4:1 tell nothing more than that in one place more energy is required than in another. All Dr. Dunning and I are concerned with, and all we can discuss, is the proportional use of energy, not what kind or how.

Dr. S. Bernard Wortis: I ask about vitamins in brain tissue because recent work by von Eüler and Malmberg on the vitamin C content of the brain of animals points out the close relationship of this substance to the oxygen consumption of brain tissue. The brain and the spinal cord tissue of young animals have a higher oxygen consumption than those of older animals (Wortis, S. B.: *Am. J. Psychiat.* **93**:87 [July] 1936), and von Eüler and Malmberg have shown recently that there is more vitamin C in the brain of the young animal than in that of the adult. This may be only an incidental relationship, or it may have important functional significance; I brought up this question of the vitamin and the enzyme content of the brain because I wondered whether any of these data on circulation of the brain could be correlated with it.

Dr. H. G. Wolff: I cannot make any correlation.

Emotional Factor in Disorders of the Skin. Dr. Eugene Traugott Bernstein (by invitation).

Personal observations are recorded illustrating the importance and frequency of the emotional factor in disorders of the skin, a subject that apparently is receiving greater attention in the postwar period. An attempt is made to show that there is a definite field where dermatology and neuropsychiatry meet and that cooperation between these specialties can be mutually profitable and instructive. A convenient classification of the eruptions primarily or secondarily related to emotional disturbances is suggested: (1) disorders of the skin in which any emotional factor may be considered secondary or incidental, (2) dermatoses of organic origin in which emotional reactions are intense, (3) neurodermatoses produced by manipulation under emotional stress and (4) frank psychogenic eruptions in which the vasomotor changes in the skin are the outstanding phenomena. The criteria for the establishment of true psychogenic dermatoses are considered critically. The principles of treatment are discussed chiefly from the standpoint of suggestive therapy, and certain common pitfalls and problems are mentioned.

DISCUSSION

Dr. Bernard Sachs: I have undertaken a considerable task in opening the discussion of this subject, but I think Dr. Bernstein has done well in bringing this problem before the members of this society. The connection between the sympathetic nervous system and these various cutaneous manifestations calls for a different line of investigation in the future, which may lead to further advances

in knowledge of the entire subject. I recall that about fifty-four years ago the relation was still a matter of serious doubt. At the time, I was a student and attended the dermatologic clinic of Kaposi in Vienna. I recall the case of a celebrated author who claimed that when he saw a lobster painted on canvas, urticaria developed.

Many cutaneous manifestations of nervous diseases are so well known that there is no need to prove the existence of these conditions, nor is there any reason to doubt their psychogenic origin. I have had serious doubts, however, whether many of the cases of supposed psychogenic origin were purely psychogenic. In the majority of such cases I have observed that the condition is more than probably due primarily either to infection or to an allergic condition. In one case, for instance, the illness began after a stay in a small village in Sicily; there the woman acquired a peculiar eruption of the skin, which persisted for many years; it was unquestionably aggravated by purely emotional influences. In another instance a woman had had an attack of ptomaine poisoning after a visit to Egypt six years before. The effects of this poisoning and the erythema persisted for a number of months. The ptomaine poisoning has long since disappeared, but any strong emotional factor is likely to produce the erythema.

Dr. Bernstein did not refer directly to angioneurotic edema, though I am certain he had it in mind, and I wish that he as a dermatologist had shown me a picture of what angioneurotic edema looks like, for no two dermatologists or two neuropsychiatrists agree as to what it is; yet its occurrence is extremely frequent. All know of the crosses that have appeared on the backs of hysterical patients and the classic stigmas and all sorts of conditions which appear in the skin after emotional excitement. A short time ago I saw a woman who said that "tremendous" rashes appeared over her body at certain times. I said: "There is nothing visible now. Where do you have this rash " She said: "I have it on my chest." On that day she was covered up to her neck, but while she was talking to me the rash appeared distinctly on her neck. She was not conscious that it had appeared there. Within a reasonably short time it paled, and it disappeared before she left the office.

I shall not discuss the therapeutic problem, for I do not know that all would agree on any one psychotherapeutic method. I am more interested in the question of causation and the mechanism by which this curious interrelation is brought about. Dr. Bernstein has referred to the group of chronic disorders. These are the most troublesome. I feel rather encouraged not only in view of the paper by Dr. Dunning and Dr. Wolff but because other recent investigations that have come to my knowledge indicate that many of these problems will not be answered merely by solving the question of the participation of the sympathetic nervous system. I believe that promising chemical and physical problems now in the process of study will throw light on and help in the solution of some of these interesting questions. In the vast majority of cases the proper psychic treatment of the patient is perhaps the most important therapeutic measure that one can apply.

Dr. Smith Ely Jelliffe: I had no intention of saying anything, but Dr. Sachs' autobiographic note stimulated a similar reaction in me. When I came to New York as a neurologist in 1894, one of the outstanding dermatologists in the city, in looking around for a bright young man, hit on me and induced me to present a paper before a dermatologic society on the relationship between the nervous system and the skin. Thus, my introduction in this city was along this line. I shall always remember with pleasure and gratitude Dr. Fordyce's introduction and continued friendship, in that he gave me the first four volumes of the *Nouvelle Iconographie de la Salpêtrière* which he had in his library. Dr. Fordyce started out to become a neurologist and became a dermatologist. The fact seems of little pertinence, except that one of the foremost neurologists, Pearce Bailey, started to be a dermatologist and became a neurologist.

Many years after, in reading an article by Montgomery, of San Francisco, who is well known to dermatologists, I was struck by an interesting remark that he repeatedly reenforced: that the skin is a "microcosm of the macrocosm." Within

the skin one may read the life history of the entire body. That thought has always remained with me and has kept alive my interest in dermatology, in its relationship to psychiatry.

Dr. Sachs has spoken of the interrelation between infection and some of the dermatoses. (Some may remember a report on the treatment of a severe compulsion neurosis which I published in 1911. A good result took place. Among the symptoms, however, which were not mentioned in the history was persistent dermatitis of the hands, which was a relic, as it were, of the patient's sadism. She was constantly hitting her hands against everything, constantly keeping up a definite, disagreeable, uncomfortable and unesthetic reaction in her hands; even after she recovered from the compulsion neurosis, the old dermatitis of the hands persisted. She would come to me every once in a while and say: "What can I do with these hands?" I said: "Stop hitting things," but it was not until I finally said: "Go to Dr. Fordyce and take a few roentgen treatments" (for I was convinced that there was infection) that the hands improved; after two roentgen treatments the dermatitis disappeared.

Dr. Sachs has also spoken of angioneurotic edema. I should have liked to hear more about it, for sometimes one observes cases of severe angioneurotic edema; I am convinced that the psychogenic component plays a large part in it. Sometimes it is extremely complicated. One case was of great interest to me. A young married man, with no children at the time, used to have severe attacks of angioneurotic edema, in which the throat was also involved; at times he almost died. Once or twice he had to have a tube passed because of the difficulty in breathing resulting from the edema. I had no chance to analyze him, but I knew that there was a definite relationship between his oral-anal sadistic attitude and the edema and discussed this with him. Mathematics was his forte. Then he had appendicitis. I was called by the surgeon and saw him as a friend. At first, I said I did not know whether it was a case of operable appendicitis or whether it was an exacerbation on the part of the oral-anal sadistic reaction occurring in the gastro-intestinal tract. I advised waiting a little. We did not wait more than six hours, however. The symptoms, including blood counts, indicated distinctly suppuration of the appendix. The operation was successful, nearly ten years ago; since, the patient has had no more angioneurotic edema. He was castrated and gave up something. This the psychoanalysts will grasp.

Two points in the presentation interested me. I should, if it were possible, like such blanket terms as "emotional" to be more carefully utilized. The emotions are highly complex and phylogenetically very old. No one thing is an emotion. There are innumerable emotions, with innumerable nuances. Without a careful psychoanalytic appraisal of the so-called emotional reactions, one says little when he speaks of "emotions." Emotions should be shown in their relation to the repressions and inhibitions of the Oedipus complex. Finally, to mount my particular hobby, with reference to certain of the suggestions that Dr. Bernstein made, especially that one must always be sure the condition is not "organic": That term does not mean much in terms of functional relationship between synaptic junctions, oxygenation and increased blood supply, to revert to Dr. Wolff's presentation. Every one knows that if one has to jump over a junction (a ditch, if you will), he has to use more energy to do it, and, if the Waldeyer hypothesis with reference to the synapses, and not the Bethe fibrillar hypothesis, is correct, there must be more resistance at the synapse, and more energy is required to pass over the synapse; therefore, there should be more vascularity. In any event, the use of the term "organic" in the sense in which I am interested as a neuropsychiatrist comes to this: An organic disease of the skin can result from psychogenic causes. This means the persistence of a specific type of emotional reaction which finally overcomes the reversibility in the biochemical processes underlying the integrity of the skin. Reversible biochemical and histologic processes become irreversible, and then there is "organic" disease.

Dr. A. A. Brill: Dr. Jelliffe is the only psychoanalyst in New York who has devoted himself to the psychoanalytic study of conditions of the skin. I fully share Dr. Sachs' wish to know what the actual mechanisms of such manifestations

are. I was much interested in the case cited by Dr. Sachs—the person who showed a cross on his shoulder. I know of such conditions, which are often designated as stigmatization. Jacobi reviewed the history of cases of this kind, citing a few hundred instances of stigmatization from the beginning of Christianity until the present (Jacobi, W. A. E.: Die Stigmatisierten, Munich, J. F. Bergmann, 1923). As late as the 1880's, when the case of Louise Lateau was so much discussed, Virchow said that it could be only a miracle or a swindle, and it was naturally concluded that, as there are no longer any miracles, the case was a swindle. There is the case now of Thérèse Neumann, who is still living in Konnersreuth, Germany, and who shows stigmatization and other so-called mystic phenomena. She was examined by neurologists and psychiatrists, some of whose works I know. Thus, A. E. Hoche examined her thoroughly; he, like some others, came to the conclusion that there was no swindle about her stigmatizations. When I first read of this, I was more or less puzzled, but a little reflection convinces one that such phenomena can come about as a result of mental processes. Thus, I reported before the joint meeting of these societies (Jan. 9, 1934) (Psychic Suicide, ARCH. NEUROL. & PSYCHIAT. **32**:880 [Oct.] 1934) the case of a woman who suffered from gastric bleeding, which was believed to be due to ulcers, but who had had no ulcer. Analysis showed that the bleeding was vicarious menstruation. She would have been operated on if she had been strong enough, but as she was in an almost moribund state, I was urged to take care of her. She has shown no signs of gastric ulcer for over two years. The question that arises in the minds of those who have been trained in physiology is how the blood comes to the surface, either in the form of stigmas or in the vasomotor manifestations described here by Dr. Bernstein. For many years I have been convinced that such phenomena occur on a psychic basis. I have seen such conditions, and others have described them. Two years ago I found a paper by Jürgensen on *"Okkulte Hautblutungen"* (occult bleeding of the skin) in which he discussed the physiologic mechanism of such bleeding. As a psychoanalyst, I explained the phenomena of stigmatization on the basis of identification. In a paper I said: "If a modern psychoneurotic can develop hemoptysis as a vicarious menstruation through identification, there is no reason why devout psychoneurotics cannot produce stigmatization through identification with the Savior." Sensitive persons can do that on a psychogenic basis. Moreover, one knows that the skin is the greatest erogenous zone and that any affective disturbance shows itself in the skin. Take the case described by Dr. Sachs, that of the woman who unconsciously produced urticaria extending from the covered chest over the neck. I saw a similar patient, who is also known to Dr. Jelliffe. She could produce the eruption at any time, whenever an emotional situation of a special nature came up. Psychoanalytically, I interpreted this manifestation as a form of showing off; she was a strong exhibitionist. Dr. Sachs surely would not think of such things.

DR. S. BERNARD WORTIS: In the study of cutaneous lesions complicating neuropsychiatric problems answers to five problems appear necessary. One should ask oneself: (1) What (substance or situation) produces the lesion of the skin? (2) What meaning has it to the patient? (3) Why does the person react in this fashion? (4) What use, if any, does he make of it? (5) By what psychoneurophysiologic process is this cutaneous lesion produced? These are the problems which I think one should try to answer specifically for each problem and one should speak wherever possible of the specific metabolic disturbance and the specific emotional disturbance involved and try to establish a causal relationship. Persons can be allergic to proteins or to life situations.

DR. JOHN A. P. MILLET: I have had a little experience in cases of this type. There is a case which I think of in this connection which brings up an interesting problem so far as the relationship between the physician and the patient is concerned and to which Dr. Bernstein referred. This case was described to me by a dermatologist. A young woman suffering from psoriasis used to come at intervals of from three to six months to this physician for treatment. The treatment consisted of application of ointment of chrysarobin—a very unpleasant remedy.

She would take this for a while and rub it on faithfully and then report the disappearance of the psoriasis. Finally, she disappeared from the physician's office and did not come again. Five years later he had a telephone call from the patient, reporting that she did not know whether or not he would be interested to hear from her but that she felt inclined to make a report. She said: "You may not have heard that five years ago I was divorced from my husband. I knew for a long time that the psoriasis was based on an emotional disturbance, though I did not tell you about it. You see, I did not like having intercourse with my husband. When I had to be at home with him, I found myself breaking out in psoriasis, and then I would come around to you for treatment. As long as I was staying at home, I was getting treatment and was not able to have intercourse with my husband because of the chrysarobin. When I went away on a trip, the psoriasis cleared perfectly, and I had no more trouble." That is self-explanatory. It is a diagnosis on the part not of a dermatologist or a neurologist but of the patient. It is interesting to speculate on the use of chrysarobin ointment by the dermatologist. It is perhaps one of the most unpleasant medications which any one can use, and I wonder whether this does not interfere with the otherwise pleasant relationship which I am sure Dr. Bernstein must establish with his patients suffering from psoriasis and which he has shown tonight to be a prerequisite for successful dermatologic practice.

Dr. Eugene Traugott Bernstein: I wish to point out that it was my purpose in this paper to record clinical data in cases of psychosomatic relationships and to show that in some instances of regular daily practice there is a link between psychiatry and dermatology. However, it was not my intention to go into the moot question of the modus operandi of psychogenic neurodermatoses. This question is one belonging to experimental medicine and its allied field. I merely pointed out that the vegetative nervous system may be considered the means by which emotions are expressed as functional disorders.

I spent the past summer studying the concept of emotion (Dunbar, Helen F.: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1913, New York, Oxford University Press, 1935, pp. 435-560). The present interpretation, according to the recent literature, differs to such an extent that one is compelled to accept this term rather as a symbol used in the vernacular and, as the discussion brought out, as a broad concept.

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, Nov. 13, 1936

Frederick Allen, M.D., *President, in the Chair*

Who Are the Criminal Insane? Dr. Charles A. Zeller, Waymart, Pa.

My purpose in this paper is to discuss more clearly a subject that has heretofore been garbed in vagueness and frequently approached with considerable reservation and an attitude of fear—the criminal insane. In reviewing the scientific literature one will find little concerning criminal behavior from the psychiatric point of view. On the other hand, sociologists and psychiatrists have contributed extensively to this subject.

Consider for a moment the person who has been classified as a criminal. Does conviction of some minor offense for which he has received a sentence of one or two years or less in prison necessarily classify that person as a criminal? Crime is a violation of the public rights, and as such it may also involve violation of the rights of another person. It is not my purpose to discuss the causes of crime, but statistics show that many persons commit only one crime and after due punishment by law lead an exemplary life. Shall one, then, classify a man of that character

as a criminal? Likewise, if the same person, while serving his sentence or paying society for this one crime, becomes mentally ill and is committed to a hospital for the criminal insane, is it then fair to the man, or even to society, to classify this person as criminally insane?

Society has not reached the utopia wherein a person after release from a hospital for the criminal insane will be received with open arms. He is always looked on with a certain amount of suspicion in every community, which makes the task of adjusting himself as a useful citizen difficult indeed.

It therefore behooves psychiatrists interested in this problem to consider carefully the case of any person whom they may examine with the possibility of commitment to a hospital for the criminal insane in the offing, and to take cognizance of his mental make-up and personality before classifying him definitely as belonging to the group of the criminal insane.

Criminal personalities, or the delinquent group, are classified largely on the basis of their characteristic antisocial behavior. In this group I place all classes of delinquent persons other than those guilty of sex offenses. Among its members are the vast majority of persons with the more common types of maladjustment and misadaptation—delinquents who generally fall into the classes; feebleminded delinquents; criminals with normal mentality; criminals with abnormal mentality, and enfeebled, emotionally inhibited criminals. I have often noted that this type of personality begins to show itself early in life. A review of case histories shows that it is well established by adolescence. I should say that about 50 per cent of criminals usually exhibit evidence of mental retardation or subnormal personality. Many of this group manifest symptoms of disturbance in the endocrine system; however, as a rule it is not possible to discover what gland or glands are directly at fault. The other 50 per cent seem to be victims of faulty social organization—the result of a breakdown in home discipline or the misadaptation of the modern educational system. In the group of queer personalities, or the eccentric group, are peculiar persons. They are usually the so-called geniuses. This group includes those having a more or less definite paranoid tendency. They are often classified as belonging to the schizoid type. I mention these personalities for the reason that in many classification schemes one can readily see how the person would easily get into trouble and violate many laws. Persons of schizoid type may go through life without breaking if they can avoid stress and strain, if they can live in a rural community and be subject to little social and economic pressure. On the other hand, if they live in a large city and are subjected to the vicissitudes of competitive economic living, many may break and, in so doing, commit some crime for which they are not responsible.

One assumes that the criminal is no different from others except in his criminal act; he is a person who could go straight if he chose to do so. However, one must take into consideration the mental factors that may intervene. If he is mentally abnormal, he should not be held responsible; according to the existing legal set-up, he, however, must be punished as an act of social revenge and as a horrible example to deter others. The man is placed in prison and made to lead a life as different as possible from that outside, without any examination or thought as to the possible mental factors that may have caused him to commit the act. Possibly the criminal is not like others, though there is no sharp dividing line between the first offender, guilty of a minor crime, and the formally law-abiding citizen who skirts the crime line closely and manages to keep just within the law. The criminal insane today is the man who has been arrested for a crime, examined by a commission and then committed to a hospital for persons of that class, without consideration of the possibility that he is a victim of defective heredity or unfortunate circumstances or both. Once convicted, the criminal must be studied carefully to find out what makes him a criminal. Only thus can one tell whether or not he can be reformed, and if so, how it may be achieved. One should no longer try to find a punishment to fit a crime—and in so doing possibly produce other criminal insane—but rather should seek treatment which will be adapted to the needs of the particular type; one need not expect that one can train a man to live well in society by removing him from the experiences and responsi-

bilities of social life. Finally, as the problem of crime stands today and until such time as one can say definitely who are criminals, it is difficult to define who are criminally insane. I cannot say that all men who are sent to prison are criminals; neither can I say that all prisoners who are committed to a hospital for the criminal insane can be considered as of that class.

DISCUSSION

DR. SAMUEL LEOPOLD: Dr. Zeller's paper is comprehensive, but I was sorry to hear him use the term "criminal insane." I have hoped that the public will some day cease to use that term. There are many persons in the world who are criminally inclined and have committed acts against the law, but have not been caught. It is only those who have been caught and found to be mentally ill that one can classify as criminally insane. I agree with the speaker that the study of these persons is practically the same, as far as their pathologic manifestations are concerned, as that of patients in the wards of ordinary hospitals for mental diseases. I wish to ask Dr. Zeller whether he found malingering frequent. I am of the opinion it does not occur often, but, to judge from the popular conception malingering is a frequent method by which a prisoner escapes the penitentiary. I saw a woman the other day who confessed that she had deliberately malingered twenty years before. She told me that in order to escape from an industrial school she had feigned insanity. She was then sent to a hospital for mental diseases, where she was discharged as well and allowed to go back to the community. She was not a normal person. I made the diagnosis of psychopathic personality. I wish to ask Dr. Zeller whether there are many feebleminded persons in the institution at Farview. The feebleminded group form the basis of the delinquency problem with which I am concerned. At the Municipal Court—where, in addition to the regular activities, my associates and I do preventive work reaching out into the lives of young children, studying them from the sociologic, psychiatric and psychologic standpoint—all persons prior to coming before the judge are submitted to a complete examination. The medical department made 8,000 examinations last year; of that number 63 per cent revealed abnormality. The feebleminded group forms the same proportion here as in any other situation in life. We study defective delinquents before they reach the penitentiary and attempt to pick up the abnormal, antisocial types as soon as possible. Another associate who is working in this field found 55 persons who he believes are potential chronic offenders; yet we know of no place to put them. The problem is not that one cannot recognize the type but how one shall handle the problem, for all institutions are filled to capacity.

DR. ARTHUR P. NOYES, Norristown, Pa.: Not having seen Dr. Zeller's paper, I was a bit curious as to how he planned to approach his subject—whether from the standpoint of definition and description or from that of motivation, or perhaps even from a medicolegal point of view. I suspect that ideas are being revised as to the incidence of mental disease or mental defect among persons appearing before the criminal courts. In a recent article in *Mental Hygiene* (**20**:529, 1936), Dr. C. B. Thompson reported that of all persons who were convicted or had pleaded guilty in the Court of General Sessions of New York City, only 1.5 per cent were found to be psychotic and 2.4 per cent mentally defective. His criterion for mental defect we hear was a mental age below 10½ years and an intelligence quotient below 70. In this connection, it is interesting that in the army tests in 1917, 7.1 per cent of the drafted group were "very inferior," a term which Thompson assumes to be the equivalent of his term "mentally defective." His figures not only corroborate the impression that mental defect is no more frequent among criminals than in the general population but even suggest that it is less frequent.

Psychotic criminals fall into various groups: those whose antisocial behavior results from the psychosis, those who become psychotic while awaiting trial and those who become psychotic during the term of imprisonment for which they have been sentenced. The first group can be subdivided into those who are, so to

speak, criminals by accident. Here one might include the patient with dementia paralytica who fails to comprehend the social and ethical implications of the behavior released by uninhibited impulses. The second group, made up of those whose antisocial acts, like hallucinations and delusions, represent efforts to deal with deep seated psychologic needs and dilemmas, is of most interest to the psychiatrist. The satisfaction of these psychologic needs is an unobtainable life goal, but the efforts to satisfy them are through various mechanisms the operation of which may result in antisocial behavior. The crime of violence may be an attempt to destroy disowned aspects of the personality which have been transferred by projection to an object invested with all the hatred which the deepest needs of the personality can enkindle. Again, it may represent an effort to magnify the ego or to defy such manifestations of authority as have become surrogates of a tyrannical father. The behavior of the criminal, like that of the socialized person, is prompted by mechanisms constituting a continuously graded series in respect to the extent to which they are psychopathologic. If extreme, they result in the offender being labeled as criminally insane, but the dividing line between the mechanisms which should be called psychotic and those which should be considered as merely psychologically unwholesome is indistinguishable. In dealing with behavior which has violated its dicta, the law, in demanding that the offender be labeled insane or not insane, responsible or not responsible, creates classifications which are largely artificial. There is no such definiteness in psychopathology. While for legal purposes such classifications are, I suppose, necessary, they do violence to psychiatric concepts. Since, too, the psychiatrist will not concede that the so-called criminal insane differ in their psychopathologic make-up from other psychotic persons, the term is one which the psychiatrist prefers to avoid. When I read the title of Dr. Zeller's paper, I wondered if he planned to discuss the McNaghten decision and the subject of so-called criminal responsibility. I am glad to observe that he has not introduced this question. Since, however, most persons are not aware how time worn this subject is, may I quote from "Lectures on Madness," written in 1873 by Dr. Edgar Sheppard, professor of psychologic medicine in King's College, London? In these lectures he commented: "They inquire of a medical witness, not whether the prisoner is of unsound mind, but whether he is in a position to know the difference between right and wrong. Dr. Blandford has well remarked, 'No more curious test of insanity was ever invented—none which more plainly shows the absolute ignorance of the subject prevailing amongst those who have no acquaintance with the insane.'"

Dr. Frederick H. Allen: I wish to say a word in regard to the title of Dr. Zeller's paper, on which both Dr. Noyes and Dr. Leopold have commented. They have wondered why the obsolete term "criminal insane" was used. This title was wished on Dr. Zeller by Dr. Lauren H. Smith and me, with a purpose. I used the word with the hope that Dr. Zeller would be able to prove through his material that there is no such thing as the criminal insane. I think that in a great deal of the material Dr. Zeller has demonstrated that this term is obsolete and should be discarded. He has shown that patients with mental illness who have accidentally committed a criminal act are no different from those who are cared for in hospitals for mental disease. Several years ago I had the opportunity of studying a group of the so-called criminal insane in one of the California state hospitals. I selected 50 cases at random, and in going over the records found that in over 50 per cent of the group there was gross evidence of mental deviation before the commission of a criminal act. This made me feel, as I still do, that the negligence of a community allows a patient with mental disease to stay in the community until he becomes dangerous. The regular machinery for handling these patients is still cumbersome. There has not yet been worked out a medically oriented legal procedure to deal with persons with mental disease, who first come to the attention of the authorities because of a criminal act.

Some patients with mental disease are much more aggressive and potentially more dangerous than others. These are the persons who are most likely to commit criminal acts. They need a more specific type of care, but it is a mis-

take to think of them as "criminally insane" and to set them up as a separate group; they are not different from a large number of patients sent to the wards of hospitals for mental disease.

DR. C. A. ZELLER: I am glad Dr. Leopold raised the questions concerning the "criminal insane." There are three classes of patients at the Farview State Hospital. All are committed through the courts but are classified for convenience. They are: the insane criminal, the criminal insane and a few civil patients. Insane criminals are men who have received sentences and have been sent to the penitentiary and then transferred to Farview. When a sentence has expired, the classification must be changed to that of the criminal insane. Other men are classified as criminally insane who have been declared insane by a commission before trial. Civil patients are sent from every civil institution in the state because they present problems that the hospitals cannot care for.

With respect to the term "criminal insane," this has been removed from all records, and the institution is now known as the Farview State Hospital.

There have been few cases of malingering; in the past six years I have seen only about 3 instances. As soon as malingering is detected, the man is returned to the county court for sentence or trial.

In discussing feeblemindedness in relation to this problem, I did not intend to give the impression that it is a basis for all crime; however, defective delinquents must receive serious consideration in the future. At present, Pennsylvania has no institutions in which they can be confined and they constitute a vicious circle by coming continually before the courts.

I have done considerable hedging as to who are the criminal insane, for as yet no one can tell definitely who is a criminal. I am inclined to think at this time that the "criminal insane" are no different from psychotic patients in civil institutions, except that possibly they may have homicidal tendencies; in many cases I have learned that the patient had had a psychosis for a time, which was not recognized.

PROBLEMS OF PRISON PSYCHIATRIC SERVICE. DR. PHILIP Q. ROCHE.

Dec. 1, 1936, marks the biennium of a formal psychiatric service within the Eastern State Penitentiary, the first of its kind in the Pennsylvania system. The employment of a psychiatrist represented one of the last movements of those establishing a classification system of case work within the prison. In the past the services of a psychiatrist were obtained only through the channels of occasional consultation and at best embraced only the semblance of standardized examinations; they fell far short of any comprehensive survey of the prison population.

At the outset the psychiatrist was met with the challenge of numerous petitions for readings of inmates who had established reputations for queer behavior but had never been considered mental problems from a disciplinary standpoint. It was remarkable to discover the number of inmates who had been sequestered for many months, even years, who were acknowledged to be dangerous, eccentric or queer and were tolerated as nuisances but who had never been examined sufficiently to determine the mental status or proper disposal. Consequently, by way of a general purge, a large contingent of inmates was transferred as mentally diseased to the Farview State Hospital during the first twelve months. This group numbered about 60 men, among whom could be counted many from the ranks of paranoid agitators, misconduct repeaters, deteriorated epileptic patients and perverted derelicts. In previous years the number of men removed as mentally ill varied from 9 in 1929 to 25 in 1934 and during these six years aggregated a total of a few more than 100. This group certainly did not represent all the mentally disordered among the prison population, as is borne out by the results of the psychiatric housecleaning which took place in 1935. Such action had a salutary effect, by reason not only of clearing the atmosphere for routine discipline and making conditions more livable for the mentally normal prisoners but of removing personal dangers to officers and fellow-inmates. In addition to the initial task of segregation and disposal of psychotic inmates,

there arose the problem of management of a rather imposing group of persons with what may be designated "borderline" conditions, few of whom under present conditions are committable as insane but who constitute a vexatious problem of prison administration. Of these there come to mind the mentally defective and the epileptic prisoners and the group of neurotic and psychotic inmates who are a constant source of friction by reason of their emotional instability manifested in prison agitation, perversions, quarrels, heedless resistance to authority, malingering and functional disorders. Previously, the task of dealing with this malevolent group was left mainly to the devices of individual guard personnel or was dismissed through the avenues of repressive discipline. This is to a large extent still true.

At present, in the prison file of psychiatric patients about 430 records have accumulated, 90 of which are those of inmates removed as insane. It must be emphasized that the accumulated records of psychiatric patients represent only 14 per cent of the population of about 3,000. No attempt has been made to study the entire population. Instead, there has been a selection, limited in volume to the departmental capacity of one unassisted psychiatrist.

The psychiatric service forms an integral part of the present program of classification in the Eastern State Penitentiary. The method is that of the case work approach; it anticipates individualized diagnosis and, importantly, individualized treatment of the inmate. Such a program is laudable in intention; yet I believe that it is disappointing in achievement. Good results are wanting because facilities are lacking for carrying out treatment. Classification is defeated at the outset by limitations of space. To shift a prisoner of one kind requires the removal and shifting of another. I am reminded of the proposed Cumberland Valley Institution, which is to be created for the purpose of absorbing the classification residue of criminal defectives. Until the Pennsylvania penal policy is expanded to meet the problem of segregation, classification will not come up to expectations. The psychiatric problems as related to the Eastern State Penitentiary may be discussed under the following heads: (1) discipline, (2) parole and commutation and (3) relation to the courts and criminal procedure.

1. *Discipline.*—The Eastern State Penitentiary consists of two units: the Philadelphia institution, known as Cherry Hill, which was built in 1824 and is equipped with 944 cells, and the Graterford institution, begun in 1923 and partly completed in 1931, which is modern in design and appointments for a capacity of 1,700. Cherry Hill is the institution of general reception and retention of the more refractory men and of those serving long terms. It is overcrowded, there being only one cell for every one and a half inmates of the general population. It is called a maximum security prison. The Graterford institution is considered a medium security prison and domiciles the better behaved and those serving short terms. Within these two walled structures are confined about 3,000 men. In a period of twelve months about 900 men come in as new admissions, and about the same number are discharged, paroled or transferred. Of the total population, about one-half are men under 30. Of these, 135 are from 16 to 18; 310, from 18 to 20; 478, from 20 to 25, and 699, from 25 to 30. Here is the genesis of the problem not only of discipline but of treatment; here is a confused world of defeated youth, of impulsive, untrained, anonymous, callow striplings and of guileful men, prematurely old at 30. Of the entire group, about 1,000 represent first convictions, but not all first encounters with the law; 1,123 men (one third of the prison population) will be confined for at least five years, and 573, for at least ten years; 85 may serve at least twenty years, and at present 236 inmates are sentenced for the remainder of their natural lives. Exclusive of those serving life terms, minimum sentences represent fifteen thousand years. In this composition are 469 men who have taken life, 145 who have ravished and 1,921 who have been convicted of major crime from two to six times prior to the present incarceration. Thus are created the ingredients of a social consciousness within the prison walls—a fellowship of the antisocial and of those with sullen resistance to reform. This social consciousness of the

physically unattractive, the defective delinquent, the psychopathic, the paranoid, the feebleminded and the lazy and vicious is perhaps akin to the herd instinct; it is the yielding of the individual to the pressure of the mob, expressed in conformity with the false bravado standards of the "big shot," in fear of being called a "squealer" or a "rat," or in the wanton destruction of property. One may cite instances of men who have immolated themselves for months at a time and in whom the most wretched obsessions have developed from fear of reprisal. It is the eye for an eye justice of the jungle, and it is real. To the mass of inmates the uniformed guard staff is the symbol of unreasoned repression. The guard is a "screw," and the moment the inmate changes his attitude and looks on the guard as an agent of his redemption, he must forsake the mob and be prepared to suffer its contempt, to lose caste and even to run personal risks; an attitude of resistance is supported by the mass conviction that men can be bought and that justice is a gamble of the biggest rewards to the biggest stakes. These are aspects of prison discipline which one cannot reduce to statistics. The better class of inmates do not yield to this influence, but the better class is only a fraction of the population and does not need solicitation. It is commonplace to hear a young inmate say in reply to importunities for reform: "I have to live with these men, and you don't." There is also the element of fear, which pervades the prison and nourishes prison neuroses and acute psychotic episodes. Again, there is the demoralizing influence of men deprived of normal libidinous outlet, physically compressed together, enervated by idleness and stimulated by the sexually aggressive. The younger men become the targets of perverted romantic overtures of the "wolves" or are stigmatized by sobriquets from the homosexual argot. Once christened, it is hard to forget. It is part of the burlesque humor of prison society. This picture as a whole is reduced to its lowest common denominator when one learns that two of every three inmates fall below the mental age of 13. Here is a small, uncomprehending world of turmoil, of violent collisions—amoral, vulgar, aggressive and childish.

Prison discipline cannot be effective without segregation. At present segregation is inadequate by reason of the physical limitations of the prison. There is no equipment for the care of the mentally disordered—either for the treatment of acute transient psychoses or for the temporary care pending transfer of those who are committable mentally abnormal. White and black persons may be separated without difficulty; the better prisoners may be transferred to Rockview or Graterford; the hardened intransigents may be concentrated into one block; yet little can be done from the standpoint of segregation of the mass on the basis of personality and educability. At present, little can be done to complement the findings of classification.

Aside from the contribution of psychiatry to case work classification, there exists an additional parallel function in the nature of a personal service to a not inconsiderable number of inmates, especially those who come for the first time and are confronted with the initial difficulties of adjustment. The psychiatrist may do much to counsel the younger element, start the novice on the right foot, forestall the development of neuroses and manage reactive depressions. For the younger inmate, one of the most difficult elements of prison adjustment is the finding of wholesome confidences. For some, the isolation, monotony, idleness and vulgar tone of prison life constitute the more demoralizing aspects of punishment. Not a few inmates who seek conference with the service for moral guidance or allied departments require psychiatric consultation for the successful interpretation of their individual problems. Thus has psychiatry succeeded, perhaps modestly, in the beginnings of individual analysis and adjustive treatment. Again, psychiatry has contributed to the disciplinary department in its management of selected cases of chronic discipline breaking. In a number of instances, punishment by solitary confinement has proved futile, and through the suggestions of psychiatry other methods of treatment have been applied, with promising results.

2. *Parole and Commutation.*—There are growing interest and appreciation that psychiatry has a useful place in the related problems of parole and commutation.

Psychiatry has touched only about 14 per cent of the inmates of the local penitentiary and only the more conspicuous abnormal behavior comes within its purview. This circumstance places both psychiatry and the surveyed part of the population at mutual disadvantage. This is understood when one learns that 18 per cent of the present group now under observation have records of previous observation in hospitals for mental disease of psychiatric agencies. This is a factor which prevents unqualified endorsement for release. Those who have escaped psychiatric scrutiny may or may not have similar disquieting histories or grievous personality defects; yet they may succeed in getting release, without official knowledge and challenge. Again, case work analysis and psychiatry are met with the problem of establishing scientific standards of comparison and judgment and with the task of creating an unequivocal idiom which is understood by and acceptable to all the agencies that take part in the liberating and granting of parole or commutation. I can think of no better example related to this need than the patient who was refused commutation because of the confusion of minds on the term "emotional instability," which was used to describe in part the inmate's personality, but not with the intention that the term should be construed as sufficient and sole grounds for refusal or, other factors considered, that it indicated a grievous defect which could not be tolerated in society. It is obvious therefore that for psychiatric service to be effective, every inmate, not an adventitious few, should have a complete psychiatric examination and that the recommendations should follow standard, unequivocal language acceptable to those responsible for final disposition. In this connection it may be proper to mention that the term "psychopathic personality," which abounds in psychologic reports and which I have employed on some occasions has been the vehicle of abuse and misuse.

My experience with parole and commutation has been difficult. Notwithstanding the machinery available for case work analysis of the patient, there remains the confusion that comes from lack of principles on which to make equitable judgment on the basis of personality, history, circumstance, observation and sponsorship. The remedy will come, I believe, when penal psychiatry finds greater acceptance and when legal institutions are more reconciled to science.

In discussing the relation of psychiatry to the courts as it has touched the prison problem, I recall the recently adopted resolution by the Criminal Law Section of the American Bar Association: (1) "that no criminal be sentenced for any felony in any case in which the judge has any discretion as to sentence until there shall be as part of the record a psychiatric report"; (2) "that there be a psychiatric service available to every penal and correctional institution"; (3) "that there be a psychiatric report on every prisoner convicted of a felony before he is released," and (4) "that there be established in each state a complete system of administrative transfer and parole and that there be no decision for or against any parole or transfer from one institution to another without a psychiatric report."

The reference to these proposals should invoke interest in records of felons transferred as mentally diseased to the Farview State Hospital. Among the 90 inmates thus transferred there were only 2 whose records indicated that in their cases psychiatric examination prior to conviction was utilized by the court. It is also of interest that 15 per cent of patients in this psychotic group had previous records of hospitalization for mental disease; yet to my knowledge such records were not made use of by the convicting authorities. A record in point reveals that an inmate was paroled from the Eastern State Penitentiary on Dec. 22, 1933; two days after release the police were called because the parolee, attired in women's clothing, was chasing people out of a house. He was removed to the Philadelphia General Hospital and subsequently transferred to the Philadelphia Hospital for Mental Diseases. He escaped and was not heard from until his release from a New York state institution for the criminally insane, on extradition to Philadelphia. On his arrival it was necessary to recommit him to the Farview State Hospital. I hesitate to estimate the cost to the public of dealing with this criminal, and probably many others like him.

After acquaintance with the psychotic group, one cannot escape the belief that about 15 per cent of the patients have an undetected psychosis responsible for the crime, which in some instances was homicide or a sex offense. The history of one inmate suggests chronic alcoholism, with the development of delusions of infidelity which culminated in the murder of the spouse and the supposed lover. I am reminded of other inmates who have been confined in hospitals for mental diseases, training schools for the feebleminded or colonies for epileptic patients. A feebleminded inmate, convicted of sodomy, was at one time confined to the Harrisburg State Hospital. Another, a rapist, twice confined in the same institution, was convicted and sent to the penal institution, to be detained only long enough for the psychosis to recrudesce. Only recently a psychotic imbecile with active syphilis was admitted to the penal institution, although there was a record of repeated commitments to and escapes from institutions for mental defectives during the ten year period prior to 1933. Another recently admitted inmate was probably actively hallucinated at the time of his crime, which was homicide. Again, another had a long history of spells of depression, and his career of several years in the penitentiary has been marked by alternating quiescence and psychosis. He was belatedly disposed of shortly after the establishment of psychiatric service in the prison. These are a few examples from a record of long recital.

One may ask what part psychiatry may play in this picture. In summary, one may say that the task of psychiatry is to contribute its judgment to the means of segregating these compressed, discordant elements, to the end that the rehabilitable may be spared contamination from the unrehabilitable. Psychiatry should lend its counsel to the problem of establishing uniformity in state-wide penal management. At present in Pennsylvania, there may be within an institution not only different schools of penologic doctrine and technic but confusion as to which shall sponsor classification and prevail. It is not an exaggeration to say that the scientific psychologic data so far accumulated have the character more of the esoteric and even less of science. There is no established policy of authoritative guidance. Psychiatry should lend its influence to the end that further development in the penal building program shall adhere to that of practical segregation. In this respect, a substantial advance will be gained with the completion of the Cumberland Valley Institution for defective delinquents. Psychiatry not only may remove psychotic patients and segregate inferior goods but can assist in the adjustment and prevention of mental conflicts. It can counsel and impart understanding. Psychiatry should endeavor to establish its worth as an auxillary to the courts and legal machinery. Lastly, psychiatry should accept the challenge of criminalism as a problem for the investigation and analysis of one aspect of mental life.

DISCUSSION

Rev. Linn Bowman (Eastern State Penitentiary): I have no contribution in a psychiatric sense. Dr. Roche directs attention to the problem of discipline. Ninety men were transferred to the Farview State Hospital. A large number of this group, about 90 per cent represented the rioting group in the last two outstanding riots at the penitentiary. I remember the passionate plea of Dr. Leopold, eight years ago, that there might be a place for a psychiatrist in the particular problem of classification. Dr. Leopold was defeated because there is no possibility of classification when there are 644 cells and 1,400 men in the same institution. Classification was impossible because of the necessity of constantly placing new men in the cells from which others are released or paroled. The only answer is a small unit institution, which I hope psychiatry will be the instrument in introducing. It has been my pleasure to visit the meetings of the Pardon Board in the last two years; one of the most important reports asked for by the board members in cases of questionable nature is that of the psychiatrist. In one court room in this city 49 cases were unscientifically disposed of in a period of nine hours—many of the convicts being sent to the Eastern State Penitentiary. One woman came to me about her son—accused of about fifty forgeries. This mother had a letter from the Superintendent of Public Schools of Camden, N. J., stating that the boy was defective in school. I took the letter to the court at the

time of the trial, but the judge sent the man to the county prison for six months. It is my hope that, before I am compelled to retire from the service of the penitentiary life of this state, I may see psychiatrists lead the way in the creation of an institution for feebleminded delinquents.

MR. THOMAS HARRISON: Does Dr. Roche think of segregating all convicted criminals under 21 years of age into a group? What is his reaction to that type of segregation? Would it help in the mental make-up?

DR. E. P. SHARP: In the terminology of the convicts, I think there is a definite and practical place for a "nut" doctor in the penitentiary. I have seen the need exemplified in many ways. There are a number of men who, of their own volition, seek the counsel of a psychiatrist. I would take issue with one point mentioned in Dr. Roche's paper. I do not think it is necessary to have every inmate in the institution examined by a psychiatrist. Psychiatrists should concentrate on the cases of inmates who are in greatest need of treatment. I should prefer that highly trained and better paid psychiatrists serve this group rather than a number of poorly paid psychiatrists trying to cover the mass population.

MR. ALBERT FRAZIER: I am impressed with the emphasis on doing away with the term "criminal insane." There are many more dangerous men in the hospitals for the mentally diseased than in prisons. Man lives by symbols—it seems to me no greater contribution is to be made than to do away with that category.

DR. SAMUEL LEOPOLD: Dr. Roche has made an excellent contribution. There is great need for placing psychiatry on the map, as far as penal institutions are concerned, and for all to get back of him in order to help carry out such a program. In this state there has already been established a program of psychology, and its influence has permeated here to the East. The problem is to see that psychology does not dominate the situation and to insist that psychiatry be emphasized as much as psychology.

DR. PHILIP G. ROCHE: I wonder how many years and riots would be required to displace the psychiatrist? In reply to the question as to the advisability of segregating into one group all offenders under 21 years of age, I may remind Mr. Harrison that such segregation is already employed in Pennsylvania and is carried out by commitment of all young first offenders to such institutions as Glenn Mills and Huntingdon. I suspect that Mr. Harrison's intention was to suggest that selected groups of persons under 21 years of age be separated. It seems to me that merely classifying persons in terms of age is to defeat one's purpose. Regardless of age, one should attempt to determine whether the man is rehabilitable and to devote institutional measures to that end. If he is not rehabilitable, it makes little difference where he is placed, except that he be kept away from the rehabilitable. I emphasize this again and hope that I have presented the mass psychologic picture of the unsegregated prison population and how it constitutes factors of resistance to reform and of handicaps to the rehabilitable group. One cannot look on the prisoner as a mere unit. On the contrary, he is unique and an individual on whom one must bestow an individual approach and an individual means of dealing.

With reference to Dr. Sharp's remarks, I cannot accept his point of view that the function of psychiatry should be limited either in number or in participation in prison problems. Psychiatry can do more than serve merely as an expedient for improved housecleaning. One must look toward a comprehensive program, uniform and effective, not only in the Eastern State Penitentiary but in all other state institutions. As I mentioned before, well intentioned as the classification is, it has not fulfilled its aims. Competent as professional workers are, there is no bringing together of their knowledge into understandable and practical form. I question whether the pardoning authorities at Harrisburg read or understand the statistical reports they receive. At present, the various departmental agencies which take part in classification are under no definite guidance or doctrinal leadership. As a consequence of this, estimates of individual prisoners are at variance, and confidence in the judgment of the case work group is not

sustained. I believe that one must look to psychiatry for competent leadership, in order to carry out such a program. The prison classification is essentially a medical problem, and the medical profession should address itself to the task. I wish also to emphasize that the inmates themselves have natural confidence in the medical rather than in the lay professional man. I wish to thank Dr. Leopold for his counsel and guidance in the establishment of psychiatry and for his remarks.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Nov. 19, 1936

STANLEY COBB, M.D., *Presiding*

MANNER OF VASCULARIZATION OF THE BRAIN OF THE OPOSSUM. DR. G. B. WISLOCKI and DR. A. C. P. CAMPBELL.

An unusual pattern of the blood vessels supplying the brain and cord of the opossum (Didelphys virginiana) has been observed. The blood vessels enter the substance of the brain and cord in pairs, consisting of an artery and a vein. These continue to branch in pairs down to, and including, the capillaries, which consist of threadlike terminal loops. Neither the paired vessels nor the terminal capillaries anastomose with other similar vessels. The brain is supplied consequently by distinct and separate vascular units which do not anastomose with one another. The units consist of end-arteries in the sense of Cohnheim, with the additional feature that the ultimate capillaries are also end-vessels. Although the capillaries of adjacent systems do not unite, the capillary loops of contiguous units interdigitate freely.

The pattern of the cerebral vessels in the opossum differs from that of all other mammals investigated. The capillaries in the latter, as is well known, form a rich network. The only configuration of cerebral vessels similar to that found in the opossum has been observed by Schöbl in lower vertebrates—in lizards and the urodelan amphibia.

DISCUSSION

DR. S. COBB: I have been especially interested in this subject for a number of years. I have worked on cats and rabbits in this way. I have always thought that there was anastomosis of these vessels in all mammals, and I was wrong.

DR. T. J. PUTNAM: Is this arrangement parallel to some extent to that of capillaries in the nail bed? Is there any similar arrangement in fishes and amphibia?

DR. DONALD GREGG, Wellesley, Mass.: Dr. Frederick Tilney has made an extensive study of myelinization in different animals and has observed a certain correlation between function and myelinization. For example, the guinea-pig is able to function at birth more than the rat, and myelinization in the brain of the guinea-pig is more complete at birth than that in the rat. What is the picture of the new-born opossum? Is there any correlation between the extent of myelinization in the opossum at birth and the unusual type of cerebral circulation?

DR. G. B. WISLOCKI: In reply to Dr. Gregg's questions, I may say that the opossum has an abbreviated intra-uterine existence, so that it is born in a very immature state. The young find their way into the marsupial pouch, where they undergo further development. The question of a possible relationship between the time of myelinization and the formation and growth of the cerebral vessels deserves investigation. Connected with this, observations should be made on the character of the vessels at different age periods.

In reply to Dr. Putnam, regarding the pattern of the cerebral vessels in various lower vertebrates: It is apparent from the work of Schöbl and Sterzi that an

arrangement of the capillaries in nonanastomotic loops, similar to what we have observed in the opossum, exists in some urodelan amphibia and lizards. In fishes, anuran amphibia, snakes and birds, on the contrary, investigations by Sterzi, Craigie and us showed that the cerebral capillaries are arranged typically as a network. The anuran amphibia, the lizards and the opossum cannot be linked in any direct phylogenetic lineage. Consequently, one must assume that the pattern of end-capillaries encountered in them is a form of specialization that has arisen independently in several groups of vertebrates. An explanation for the change from the network type of capillary bed to the end-capillary type cannot be offered.

In regard to the capillary loops of the nail bed in man: They bear some resemblance to the end-capillaries of the opossum's brain, but anastomoses in the nail bed are not infrequent. In many villous structures containing connective tissue papillae (intestinal and placental villi), the capillaries are arranged in small, elongated tufts, but anastomoses are numerous.

MEDICAL TREATMENT OF MÉNIÈRE'S SYNDROME. DR. MADELAINE R. BROWN.

According to the careful metabolic studies of Furstenberg, Lashmet and Lathrop, the amount of sodium, and not the amount of water retained, was the important etiologic factor in 14 patients with Ménière's syndrome. A diet low in sodium and large doses of ammonium chloride prevented the storage of sodium. Six patients from the neurologic outpatient department of the Massachusetts General Hospital and 6 patients from the Boston City Hospital were given a diet low in sodium, with the addition of ammonium chloride. While on this regimen, for periods ranging from six to twenty months, none of the patients has suffered a severe attack.

The paper will be published in full in the *Journal of the American Medical Association.*

DISCUSSION

DR. CHARLES JOHNSON: I have tried Dr. Furstenberg's regimen for the last few years in several cases. I have had great difficulty in getting patients to tolerate 3 Gm. of ammonium chloride three times a day. Has Dr. Brown had any such difficulty? Has she any suggestions that may help?

DR. DONALD MUNRO: Dr. Brown is to be congratulated for bringing this important disease to the notice of the society. It has been studied in practically every part of the world except New England; it has been neglected here. There are certain difficulties associated with present day treatment, of which the first is that of making a diagnosis. In 80 per cent of cases the diagnosis of Ménière's syndrome is made incorrectly. It should be "aural vertigo." The diagnosis of true Ménière's disease should be limited to the explosive attacks of vertigo in which no etiologic factor can be distinguished. The pathologic nature of the latter is therefore unknown. The variety of treatment is multitudinous. At present the efficacy of any type of treatment for true Ménière's disease should be considered as still sub judice. One should be willing to try this diet but should not necessarily expect to obtain successful results.

DR. WILLIAM N. HUGHES, Providence, R. I.: I can testify to the value of the low sodium diet, with potassium chloride rather than ammonium chloride. I have had two cases in which the treatment was successful. I refer to Ménière's syndrome rather than to Ménière's disease. There are certain other factors that should be emphasized in addition to the low sodium diet. One patient had a typical attack of deafness, dizziness, nausea and vomiting, which disappeared when abscessed teeth were removed and remained absent for several years. Later, the same patient had similar symptoms after eating lobster. He stayed well for a few years and then had a recurrence. I tried dehydration, and there was some improvement, but it was not adequate. Then I tried a low sodium diet, with 3 Gm. of potassium chloride, and the symptoms disappeared. Dead teeth without abscesses were next removed, on the theory that a dead tooth without abscess

formation might allow toxins or bacterial products to enter the body—possibly even more easily than a tooth with a walled-off abscess. After removal of these teeth, I stopped the low sodium diet with potassium chloride. The patient has had no attacks for six months. Sodium bromide was often given in the past in cases of Ménière's syndrome, but it is now contraindicated because of the sodium. I observed a case in which marked depression with ataxia resulted from the use of sodium bromide. This type of bromide poisoning is rare and was not noted until it occurred for the second time in the same patient. The first time it was thought to be due to the toxic process producing the Ménière's syndrome. Phenobarbital has a distinct place in treatment. One patient was given limited amounts of sodium chloride with calcium lactate, 10 grains (0.647 Gm.) three times a day. He has been better for one and a half years. The tinnitus has disappeared, and bone and air conduction have increased on the side involved. There is no question that the head feels different when the patient is given a low sodium diet with potassium chloride. The cases in which there seemed to me to be toxicity have been those in which attacks of vertigo lasted only seven or eight days at a time, stopped for a week or more and then started again. Ménière's syndrome occurring daily for more than eight days has proved in my experience to be due to acoustic neuroma. If there are a dead labyrinth on one side and a dead vertical canal on the other, one can be sure that there is an acoustic neuroma. Examination of the spinal fluid is of great value; pressure and the total protein content are almost certainly elevated in cases of acoustic neuroma. Head colds seem to be another factor in precipitating this syndrome, and attacks tend to appear more then than at any other time.

Dr. M. Brown: In answer to Dr. Johnson about ammonium chloride: I have had only 1 patient who had much trouble—an elderly man with hypertension and arteriosclerosis. I had to stop the administration because of vomiting. Most patients tolerate it well, although I expected trouble with such large doses. Often I tried to increase the dose gradually, beginning with one-half the dose and at the end of a week or two giving the full amount. So far as diagnosis is concerned, the accepted description of the disease includes deafness of nerve type, of no known etiology. The attacks seemed to be identical, and all patients who have had middle ear deafness for any length of time also have nerve deafness. Hence I initiated the diet, even though there had been a preexisting middle ear deafness. The patients progressed as well as those whose deafness had started from no known cause. I have used potassium chloride in place of salt, but not in place of ammonium chloride. I do not see why it might not work. Phenobarbital is often helpful. As regards the question of acoustic neuroma: Lumbar puncture was performed in many cases, and no increase in pressure or in the protein content was found. The disks were not choked, and there has been no question of neuroma in this series.

Alcoholic Psychoses in Massachusetts, 1917-1935. Dr. Riley H. Guthrie and Dr. Neil A. Dayton.

Alcoholism and its aftermath in the physical and mental fields must be included in the list of controllable and preventable disorders. During the past twenty years the United States has made an effort in the direction of the control of alcoholism, through the eighteenth amendment. We have tested the efficacy of this approach by studying its influence on the incidence of alcoholic psychoses in Massachusetts during the period from 1917 to 1935.

While various war time measures had a certain effect in reducing the consumption of alcohol during 1918 and 1919, the year 1920 marks the first year of prohibition under the eighteenth amendment. First admissions of patients with alcoholic psychoses from the Boston metropolitan area (admissions to the Boston Psychopathic and the Boston State Hospital) showed high rates (on the basis of the population) for the years 1917, 1918 and 1919. A marked drop to the low rate for all years occurred in 1920. The rates then rose, and from 1922 on they continued at approximately the same level as observed from 1917 to 1919. First

admissions to other state hospitals, drawn from the remainder of the state, revealed higher rates for the years from 1917 to 1919 and a drop to the low rate in the year 1920. From 1922 on the rates presented a series of fluctuations, on a level approximately half as high as the figures for the period from 1917 to 1919. Data on readmissions from the Boston area reveal 1920 as the low year, while the years preceding and following 1920 were on the same level. Readmissions from the remainder of the state showed high rates during the years from 1917 to 1919 and a much lower rate in 1920. From 1921 on the general level of rates of readmission was only slightly above that of 1920. Sections of Massachusetts outside the Boston area made the best showing in lower rates of admission for the alcoholic psychoses during the years of the eighteenth amendment, especially in the number of readmissions. A study of patients admitted for the first time, for every type of psychosis to all hospitals for mental disease throughout the state, and classified as "intemperate" in the use of alcohol, reveals high rates from 1917 to 1919, a precipitate fall to the low point in 1920 and a moderate rise with a flat curve from 1922 on. The number of arrests for drunkenness, deaths from alcoholism and persons requiring relief during these years showed the low point in the year 1920.

Rates for first admissions for the alcoholic psychoses at the Boston Psychopathic Hospital, from 1917 to 1935, were six times as high in males as in females. Both sexes showed high rates in the age group of from 40 to 49 years. The men showed a decreasing proportion of alcoholic psychoses for the ages from 20 to 29 and from 30 to 39 and increases from the age of 40 on. The women showed decreases between the ages of 20 and 49, a marked increase between the ages of 50 and 59 and a smaller increase from the age of 60 on. While the population was showing a similar shift to the older ages, the degree was less than half that noted for the alcoholic psychoses. Reverting to averages, the admission age for males increased 3.9 years, from 43.5 years in the period from 1917 to 1919 to 47.4 years in the period from 1932 to 1934. The admission age for females increased 4.1 years, from 42.8 to 46.9 years. Over the same years the general population aged less than 2 years.

The first year of the eighteenth amendment, 1920, showed low rates for many factors—both first admissions and readmissions for the alcoholic psychoses, the "intemperate" groups of all psychoses, deaths from alcoholism, arrests for drunkenness and the number of persons requiring relief. After 1920 the incidence for alcoholic psychoses in the Boston area resumed the high level of the prohibition era for both first admissions and readmissions; the rates for the remainder of the state remained below the level of 1917, 1918 and 1919. Reductions in admission rates for the alcoholic psychoses during the years of the eighteenth amendment were minor in the metropolitan area but distinctive in the smaller cities, towns and rural areas. During the period from 1917 to 1935 the alcoholic psychoses have shown a definite shift from the younger to the older age groups, and they are appearing less frequently in the younger ages.

DISCUSSION

DR. P. YAKOVLEV, Waltham, Mass.: What could be the factors responsible for the shift in the higher incidence of alcoholism from the younger to the older age groups?

DR. T. J. PUTNAM: Are these statistics all corrected for changes in population?

DR. F. L. WELLS: With regard to the incidence of intemperance, the matter of definition is essential. Is it not possible that now one has to drink more to be classified as "intemperate"?

DR. A. W. STEARNS: I have been much interested in seeing these data concerning alcoholism. One might ask innumerable questions expressing doubt, but it would appear that prohibition, with all its evils, did some good medically. The rebound following the low period was said at the time to be due to the building

up of illicit traffic. In other words, the prohibitionists had their law, and the people had their liquor. It is common to speak dogmatically concerning the racial factors. One could cite many instances showing the fallacy of making deductions from data concerning racial components. For instance, in the Massachusetts State Prison prior to 1840, except for a large Negro component, almost all were native born, of English ancestry. Then followed the great famine and migration from Ireland, and a large percentage of persons admitted had been born in Ireland. This has gradually been replaced by groups arriving later, until at one time there was no one in the Massachusetts State Prison, at Charlestown, who was born in Ireland. Any one studying the population there at any given time might draw erroneous conclusions from the group. The high death rate during prohibition might have been due to bad liquor. I believe that after a party in a city in the western part of the state there were 30 or 40 deaths. I am glad to see social data presented to this society; there has been progressive neglect of these fundamental phases of neuropsychiatry.

Dr. N. A. Dayton: As the admission rates for the various age groups are based on the population figures of the same ages, we may assume that the observed trends are valid and of considerable significance. It is obvious that the alcoholic psychoses are shifting from the younger age groups to the older. A simple explanation, of course, is that the persons in the younger age groups are not indulging in alcohol to the same extent as did the generations preceding them. For example, when the population now between 50 and 60 was between 20 and 30 years of age, they probably showed a high rate for alcoholism similar to their rate at present. As they moved into the older age groups they took the high rate for alcoholism with them. The younger age groups are starting out with a lower rate. One may expect that they will carry this lower rate with them into the older age groups. These rates do not point out sudden changes in the drinking habits of a generation. They do, however, point out basic improvements occurring in the population as a whole. Every graph which we have presented has been based on a population comparison.

The term intemperance was defined clearly by the American Psychiatric Association, in their statistical manual, in 1917. This manual and its established criteria have been used by all state hospitals contributing material to this study. With a clearcut definition in front of them, I do not think that the interpretation of intemperance has changed a great deal.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 19, 1936

Francis J. Gerty, M.D., *President, in the Chair*

Correlation of Oxygen Deprivation with Intelligence, Constitution and Blood Pressure. Dr. S. H. Kraines.

Gellhorn and Spiesman have found that there are changes in vision and hearing when subjects breathe concentrations of oxygen of 10 per cent or less. They did not find any changes in the auditory or visual fields with oxygen concentrations of or above 10 per cent. I have tried to determine whether any psychologic changes occur with this percentage of oxygen. The abbreviated form of the army alpha intelligence test was used. All but 1 of 30 subjects showed a drop in intelligence while breathing 10 per cent oxygen. The first division of the army alpha test showed a small increase in the score, in spite of an increased number of errors, while the last division of the test showed the greatest drop in the score. The difference between the first and the last division is explained by

the fact that the velocity of cerebral circulation is increased during anoxemia and thus counteracts the effects of diminution of oxygen in the air. Also, during anoxemia there is contraction of the spleen, which also counteracts the early effects of anoxemia by pouring a large number of red corpuscles into the blood stream. The compensation lasts only for a few minutes.

There were marked variations in score between various subjects, under identical conditions. This variation is not correlated with the type of physique.

Because of the possibility that velocity of cerebral circulation is the basis of compensation for deprivation of oxygen, 13 subjects were given 8 per cent oxygen while standing, and the blood pressure was measured every minute. When the fluctuations in blood pressure were added for each succeeding minute, the subjects who had changes in blood pressure of 10 mm. or less in the first three minutes showed a drop in the intelligence score of less than 10, whereas the subjects who had changes in blood pressure of more than 20 mm. in the first three minutes showed a drop in the intelligence score of more than 25. There were only 2 exceptions to this rule.

The material is still too limited to permit general conclusions but suggests that the ability of the brain to withstand deprivation of oxygen is dependent on the ability of the cerebral circulation to be maintained at an effective and constant level.

DISCUSSION

Dr. D. M. Olkon: In a recent study of the oxygen saturation of the blood in epilepsy, neurosis and other neurologic diseases, Lennox and Gibbs found no appreciable difference as compared with the oxygen content of the blood of normal persons.

Dr. Kraines bases his report on the artificial induction of oxygen deficiency in normal persons; as a result, there was manifestation of mental aberration and mental confusion. On the basis of these findings, Dr. Kraines suggests a causal relationship between lack of oxygen and schizophrenic manifestations. How is artificially induced lack of oxygen comparable to the schizophrenic milieu of the patient? How does the lack of oxygen maintain its fixity? The usual course in schizophrenia is protracted, and when improvement takes place, it is usually in the same environment. I cannot follow Dr. Kraines' trend of thought as to the similarity in this instance.

Dr. Charles F. Read, Elgin, Ill.: Was there any check on the basal metabolic rate in these persons?

Chronic Manganese Poisoning: Report of a Case. Dr. Albert W. Bryan, Madison, Wis.

History.—R. M., a man aged 47, had worked from 1930 to 1932 grinding ores containing manganese, associated with which there was much dust. For some months thereafter he loaded ore into hoppers, which was not dusty. Through most of the year 1935 he was again grinding ore. In 1933 he complained of aching and burning pain in the feet. Later there appeared: difficulty in walking, with a tendency to stumble; cramps in the calf muscles, especially on lying down; easy fatigue in talking, so that he became economical of words; weakness of the legs and knees; gradually increasing melancholia, so that he seldom laughed or smiled; increasing tremor of the hands, especially when sitting; headache in the frontal region, which for about two years had recurred for about two days in each month.

Examination.—On his admission to the Jackson Clinic, Madison, Wis., on July 27, 1935, the patient was well nourished, weighing 170 pounds, but was rather pale. The blood pressure was 120 systolic and 80 diastolic. The facial expression was masklike. The ocular fundi were normal. The pupillary reflexes and ocular movements were normal. Hearing was normal. Taste was slightly diminished on the anterior part of the tongue. Speech was slurred and scanning.

The hands showed tremor in movement. In heel to knee tests the movements were slow and ataxic. There was slight adiadokokinesis. Muscle strength was generally reduced, especially so in the calves, the rotator muscles of the legs, the peroneal muscles and the muscles of the toes. There was lead pipe rigidity on passive movement of the arms and legs. Sensation was normal to painful, tactile, thermic and vibratory stimuli. In walking forward, the patient took long, even steps, which were stiff, slow and deliberate and were made with obvious effort and with few associated movements. In walking backward, there was a succession of short steps, with falling backward within about 3 feet (91 cm.). In sitting down, the patient struck the seat sharply because he was unable to limit the downward movement. Emotionally, the man was irritable and melancholic. Judgment and memory were impaired. There was rapid fatigue on effort.

Laboratory studies made as a routine revealed no abnormalities in the urine, blood or cerebrospinal fluid, except for slight secondary anemia.

Determinations of Manganese: Special studies were made by Dr. F. L. Kozella, state toxicologist, of the feces, urine, cerebrospinal fluid obtained by forced drainage, blood and hair. The results were:

	Date	Total Material	Total Manganese, Mg.	Manganese, Mg. per 100 Gm. or Cc.
Feces	3/17/36	76 Gm.	2.1580	2.840
	3/19/36	37 Gm.	1.3060	3.530
Urine	3/17/36	2,625 cc.	0.0624	.....
	3/19/36	2,200 cc.	0.0660	.....
Spinal fluid	3/17/36	75 cc.	0.2500	.....
	5/13/36	.....	.....	0.046
Blood	5/13/36	.....	.....	0.022
Hair	5/13/36	.....	.....	0.018

Controls: (*a*) Twelve single specimens of cerebrospinal fluid from cases selected at random contained too little manganese for quantitative determination. (*b*) The pooled cerebrospinal fluid obtained in 6 cases in which encephalography had been performed contained only 0.03 mg. of manganese in 530 cc. (0.0056 per cent).

Conclusion: The amount of manganese in the patient's cerebrospinal fluid was more than seven times as great as in specimens used as controls, even though the findings in the blood and urine were within normal limits.

DISCUSSION

DR. E. M. MIKKELSEN: Why did not the man stagger when he made the distal turn, as he did before?

DR. R. P. MACKAY: Was Dr. Bryan able to convince himself that the rigidity was of extrapyramidal type? Was there resistance of cogwheel type in passive movements?

DR. ALBERT W. BRYAN: I cannot answer the question about staggering, but the man was always the same. I did not think that there was any element of malingering. There was a tendency to cogwheel or "lead pipe" resistance on passive motion.

TEACHING OF PSYCHIATRY TO UNDERGRADUATE STUDENTS OF MEDICINE. DR. FRANCIS J. GERTY.

For the most part, the subject-matter of psychiatry to be taught to medical students can be grouped under three headings: (1) study of the individual as a living entity, including structure and development, internal relationships and relations to the environment; (2) general psychopathology, and (3) special psychiatry.

1. Study of personality means study of biology in its widest sense, including its psychologic aspects. In this course are to be included: securing the life history

of relatively normal persons and consideration of the problems, reactions and discoverable mechanisms in such histories; study and application of special methods of testing, and consideration of remedial or corrective measures.

2. Under psychopathology are to be included: study of the person who is poorly adapted to stress, either internal or external; the phenomena—reactions—which constitute symptoms, and the method of observation, recording and organization of the reactions.

3. Special psychiatry includes a study of syndromes, disease complexes and diseases, with their classification. For several years I have used a simple grouping into amentia, dementia, psychosis, psychoneurosis and constitutional psychopathic inferiority, pointing out objections to the use of these terms, avoiding rigid definitions and making allowance for overlapping.

The method of teaching must be adapted to the subject-matter to be taught. In teaching the subject-matter in group 1, I use lectures and explanations, recording and analysis of the student's own life history and that of other persons known to him, analysis of case histories from child guidance and dispensary clinics, assigned reading, discussion of personal problems with an instructor, taking of histories of patients and performance of special tests. In the courses on psychopathology and special psychiatry emphasis is placed by the student on "doing" in the form of clerkships, dispensary work and demonstration clinics. I am also in favor of giving explanatory and coordinating lectures, in the effort to assist the student to organize his knowledge.

As to the arrangement of these courses in the medical curriculum, the material contained in group 1 is given in the first and second years, and that in groups 2 and 3, in the third and fourth years.

DISCUSSION

DR. RALPH C. HAMILL: May I ask what are the fundamentals in psychiatry?

DR. FRANCIS J. GERTY: I pointed out that there is disagreement on that. I supposed that they would be included in a list of the points I gave in the first section of the paper. I think the fundamentals have to do with the total development of the person, his reactions to things internal and things external. It is important to study the matter with regard to the normal, so that when one studies the pathologic, even though much of the mechanism is still hidden, one uses the scientific methods of observation—fact-gathering and organization of material with a view to reaching conclusions. I think psychiatry is still in the stage of fact-gathering and that what has been learned of reasonable hypothesis should be taught to students, but I do not think that debatable or fanciful theories should be taught at length, at the expense of the factual material.

DR. CHARLES F. READ, Elgin, Ill.: I wish to thank Dr. Gerty for presenting this material. It is a subject of great importance. I am interested because I have had experience in endeavoring to expose medical students to psychiatric concepts. In the last five years there has been great advance in this undertaking. There has been some increase in the contact of medical students, as interns in general hospitals, with the concept of the body-mind organism. A few teachers are progressing beyond the idea that they deal purely with the so-called physical manifestations of disease in the study of medicine. However, this movement has not yet gone far, judging from my experience with the men who come to a state hospital for a six months' internship. Probably not more than twenty of all the students who are graduated annually in Illinois take this course. This is a small percentage; those who do are appreciative of the opportunities. I believe that these internships should be encouraged. The course in medicine is long enough; comparatively few desire to spend an additional six months in a special hospital. This is something that should be presented to them much more enthusiastically than is being done at present by those who teach these subjects in the medical schools.

CARBOHYDRATE METABOLISM AND THE CONVULSIVE THRESHOLD: A PRELIMINARY REPORT. DR. THEODORA WHEELER (by invitation).

A series of sugar tolerance tests, repeated in pairs, have been made on about 20 male epileptic patients, whose ages ranged from 14 to 54 years. The Folin-Wu (modified) technic was used, and the work was done by Dr. M. R. Freeland and his assistants, in the chemical laboratory of the Presbyterian Hospital. The chief purpose of the investigation was to observe whether detectable functional differences are associated with the ingestion of phenobarbital. The usual dose was 1½ grains (0.097 Gm.), two or three times a day. As a rule, the patients entered the Presbyterian Hospital the night before the first test (I). After a variety of procedures had been tested, the order of events selected and carried out in about half the instances was the continuation of routine medication through a dose given forty-five minutes before the fasting specimen of blood was taken. The phenobarbital was then discontinued.

The second test (II) was made on the second succeeding day in 10 cases, which are considered here. A five hour test span was used, but the intervals finally decided on, i. e., during fasting and half-hour, one hour and two, three, four and five hours, were used only for a few determinations on the present group of patients.

In 27 per cent of the 310 blood sugar determinations the range was from 65 to 185 mg. of dextrose per hundred cubic centimeters of blood. Of the other 39 instances 18 were below and 21 above these limits. Much individual variation was found in the curves for the blood sugar. Concerning the point in question, i. e., whether or not the patient had received phenobarbital, the difference in all but 1 instance was flattening of the curve on the day of administration of phenobarbital. The peak was lowered, and the subsequent hypoglycemic phase or dip was less pronounced than on the day when the patient had not received medication. While differences of striking magnitude were not usually encountered, the leveling effect was judged to be of possible significance with regard to the therapeutic action of the drug in preventing seizures.

Two pairs of representative determinations follow:

		Blood Sugar Levels, Mg.							
		Fasting	30 Min.	1 Hr.	1½ Hr.	2 Hr.	3 Hr.	4 Hr.	5 Hr.
Case 12									
I (with 1½ gr. phenobarbital b.i.d.)	9/23/36	91	125	130	112	97	111	..	96
II (without phenobarbital).....	9/25/36	95	149	139	105	103	91	..	90
Case 20									
I (with 1½ gr. phenobarbital b.i.d.)	11/11/36	77	107	128	...	105	70	54.5	76
II (without phenobarbital).....	11/13/36	84	149	141	...	115	58	84	95

Blöch and Bergel (*Wien. Arch. f. inn. Med.* **26**:233, 1935) made sugar tolerance tests on 17 normal women at various times in the ovarian cycle. Each curve of this series comprised 9 determinations for a period of three hours. The first five specimens were taken at fifteen minute intervals (from fasting through one hour), and the last four were taken every half-hour. These authors concluded that on premenstrual and first menstrual days the sugar tolerance test showed a higher peak than at postmenstrual and midmenstrual times. The peak was likely to come earlier, and there was a steeper declivity to the hypoglycemic phase at these times, with a lower point of hypoglycemia. Occasionally a prolonged (plateau) phase of hyperglycemia was encountered immediately before and during menstruation.

The study of Tyson, Otis and Joyce (*Am. J. M. Sc.* **190**:164, 1935) contains additional evidence regarding this subject. They made dextrose function tests on 7 institutionalized epileptic patients who had received no phenobarbital for twelve hours prior to the test. They found normal curves in 2 patients whose seizures averaged about six a year. In 3 other patients, with seizures averaging from

twelve to nearly fifty a year, the peaks for the blood sugar were exaggerated (180 mg. or more), and the hypoglycemic phase was more depressed than normal. In 2 other patients, with an average of twenty-four and sixty major seizures a year, respectively, a further deviation from normal was observed in that the hypoglycemic dip was delayed to nearly four hours instead of occurring at about two hours, thus creating a plateau type of curve.

An initial attempt was made in 5 of my sugar tolerance tests to obtain correlated determinations of the p_H of the blood. As the absolute accuracy of the galvanometer used was not greater than 0.1 p_H and as in 4 of the 5 curves, for patients in whom no seizures occurred, all the 27 determinations of the p_H were between 7.41 and 7.46, it was thought obvious that no minor shifts or trends could be traced and that larger shifts did not exist. However, in the 1 instance in which withdrawal of phenobarbital resulted in inducing a series of eight grand mal seizures, two within three hours before and three within the first two hours of the test, when the experiment had to be abandoned, the following striking values for the p_H were obtained: Seizures occurred three hours and one hour before the time when the fasting blood sugar was 111.7 mg. and the p_H of the blood 7.42. Two seizures followed, one immediately after obtaining the fasting specimen and one immediately before the half-hour specimen was procured; in this half-hour specimen the blood sugar was 208.3 mg. and the p_H of the blood 7.68. In the one hour specimen the blood sugar was 184.4 mg. and the p_H of the blood doubtful, there being too much hemolysis for analysis; another seizure occurred at this time. In the one and a half hour specimen the blood sugar was 138 mg. and the p_H of the blood 7.57. In the two hour specimen the blood sugar was 94.6 mg. and the p_H of the blood 7.48.

DISCUSSION

DR. BENJAMIN BOSHES: I am interested in this subject because for about one and a half years I have had occasion to make extensive carbohydrate studies in a series of patients suffering from epilepsy. There was no change in the carbohydrate metabolism in these patients, if one gave consideration to the age and weight of the patients and similar factors.

As regards drawing conclusions, certain pitfalls may be pointed out. When one makes a number of dextrose tolerance tests on any person, there are marked differences in the figures. I have seen the sugar content during fasting vary from 65 to 90 or 105 mg. per hundred cubic centimeters, when the specimens were run by the same technician. This has been noted by many workers. If there is this range between one reading and another, it would seem that there is danger in attributing the change in curves such as have been presented to phenobarbital. The effect of phenobarbital on dextrose metabolism is variable, according to reports in the literature. I think the changes seen in the sugar tolerance curve are related not so much to the patient as to his available dextrose. The patient may show a normal dextrose tolerance curve on taking phenobarbital, whereas if he took sugar just before he would have a high curve. Ordinarily, when there is much free dextrose to be utilized, there are hyperglycemia and a high curve after a large dose of phenobarbital. On the other hand, if the patient has little dextrose, the blood level is lowered and the curve drops. To evaluate phenobarbital as a drug that affects the sugar tolerance curve in patients with epilepsy, one must first determine what it does in the normal person.

The hypoglycemic phase of the curve occurs in a large number of apparently normal people. There are two explanations, and I think one contains more truth than the other. Not infrequently, the one hour level will be 150 mg. per hundred cubic centimeters or more and then drop to 60 or 70 mg. or a point below the fasting level at the end of two hours. This illustrates the so-called hypoglycemic phase of the dextrose tolerance curve. It has been thought that dextrose in the blood stimulates an increased secretion of insulin and that when this burns there is still an excess of insulin in the blood, which begins to burn the rest of the dextrose and cause a lowered sugar level. The work of Soskin,

at the Michael Reese Hospital, on depancreatized dogs which were given a constant intravenous injection of dextrose and insulin would show that the hypoglycemic phase is related not to the pancreas but to the liver and that if the liver is intact, the added dextrose tends to stop glycogenesis; when the available blood dextrose is burned, the liver is still in a static state. Until the liver recovers, the subject is not securing the proper supply per minute of dextrose (from glycogen) and is therefore in a hypoglycemic state.

It is well known that some barbiturates are excreted by the kidneys, but some go through the liver. In order to establish that the alteration in the dextrose curve is related to the intake of phenobarbital, it would be necessary to prove that the drug disturbs the homeostatic mechanism of the liver.

My colleagues and I have made the same studies with bromides and have followed closely the blood sugar levels during fasting and the sugar tolerance curves; we found that from 0 to 300 mg. per hundred cubic centimeters of bromide causes no alteration of any of the dextrose levels. Certainly, if bromide produces the same effect as phenobarbital, there is some discrepancy. It would be interesting to study the concentration of phenobarbital in the blood during the dextrose tolerance study, to correlate this with similar bromide studies before arriving at conclusions. The startling thing in our series was that by injection of insulin we could drive the blood sugar down to marked hypoglycemic levels for about two hours without producing convulsions.

DR. THEODORA WHEELER: I agree with Dr. Boshes that preceding nutritional states must be taken into account, probably for a considerably longer time than I have done here. It would probably be well to have the patients under strictly controlled conditions for from two to four days or even longer. Dietitians at the Presbyterian Hospital are giving aid in educating the patients in a moderate carbohydrate and increased fat diet. This consists of 1.1 Gm. of carbohydrate, 1 Gm. of protein and 2.2 Gm. of fat per kilogram of body weight. My associates and I are not attempting to use a ketogenic diet. However, it may be noted with regard to the ketogenic diet that, in addition to the induction of ketosis, the fat molecules may act as a brake on the rapid absorption of carbohydrate, the actual quantity of which also is not high.

I do not describe phenobarbital as having a definite hypoglycemic action on the sugar tolerance test. I have rather said that it has a tendency to level the curve, lowering the high values but also slightly raising the low.

Regular Meeting, Dec. 17, 1936

FRANCIS J. GERTY, M.D., *President, in the Chair*

THE CASE AGAINST SYMPATHECTOMY FOR PERIPHERAL VASCULAR DISEASE. DR. G. DE TAKÁTS (by invitation).

Arguments against the use of sympathectomy in the treatment of peripheral vascular disease are discussed under four headings:

1. *Return of Peripheral Circulation to the Preoperative Level.*—Johnson and his co-workers have stated that peripheral circulation returns to the preoperative state from sixteen to twenty-one days after sympathectomy. My observations indicate that while vascular tonus is recovered and the vessels react to direct application of heat and cold, the sympathectomized vessels are freed from a number of extrinsic and intrinsic stimuli which reach the limb through vasomotor pathways. Thus, cooling the body, pinching, pain, fright, anger and deep breathing do not produce vasoconstriction in the sympathectomized extremity, nor will heating the body or production of fever by typhoid vaccine produce vasodilatation. The diseased vascular tree is even more sensitive to such stimuli than normal vessels. Sympathectomy puts the diseased vessel at rest. Vasoconstrictor impulses

also come to the extremity from thrombosed arterial or venous segments through a spinal reflex. The efferent path of this reflex is intercepted by sympathectomy. Such a reflex operates in Buerger's disease and in the reflex dystrophies, such as traumatic osteoporosis, Sudeck's atrophy, causalgia or stump neuroma.

Dr. F. K. Hick and I found another evidence of altered circulation in the sympathectomized limb by studying the oxygen saturation of the venous blood, which consistently rises and remains elevated after sympathectomy, provided that the organic damage to the vessels is not too advanced.

It is concluded that peripheral circulation is permanently influenced by the vasomotor paralysis following sympathectomy.

2. *Regeneration of Sympathetic Fibers.*—Sympathetic fibers readily regenerate, and restoration of their functional activity occurs. While it is conceded that regeneration of preganglionic or postganglionic fibers does take place, removal of the ganglionated trunk with its postganglionic fibers insures against regeneration, provided the last cell stations are removed. However, postganglionic degeneration is responsible for another undesirable consequence of sympathetic ganglionectomy, namely, sensitization of the blood vessels to epinephrine and other hormones. To overcome this, Smithwick and Telford have described preganglionic sections for the upper extremity, with measures to prevent regeneration. I have had limited experience with the posterior approach but have used Telford's anterior approach on sixteen occasions. Time will show the percentage of failures or recurrences after this type of operation; one can register only the marked difference in the two upper extremities of 4 patients, each of whom had a postganglionic degeneration on one side and a preganglionic section on the other.

I believe that while regeneration of fibers may occur, restoration of continuity with the spinal cord is impossible and, hence, all reflex or central stimuli to the vessels are intercepted. Hormonal influences may become more pronounced if postganglionic degeneration occurs.

3. *Vascular Diseases for Which Sympathectomy Is Performed Are Not Diseases of the Vasomotor System.*—The ganglia and fibers which are removed are usually free from disease. Sympathectomy operates not by removal of diseased tissue but by alteration of function. Fluctuations of vasomotor tonus in Raynaud's disease may be enough to close a sensitized or abnormally narrow artery. In Buerger's disease sympathectomy puts the inflamed vessel at rest and interrupts a spinal reflex originating in segmental thrombi. It has the same result in the reflex dystrophies. In poliomyelitis with vasomotor phenomena it may inhibit an efferent vasoconstrictor impulse originating in irritative phenomena of the lateral horn or anterior roots.

4. *Clinical Benefit from Sympathectomy Is Often Slight or Negligible.*—This argument calls for an analysis of the causes of failure following sympathectomy. Mistaken diagnosis, mistaken indications, improper stage of the disease for operation, faulty technic, improper after-treatment and poor follow-up are the most important causes of failure. The surgeon performing sympathectomy must be thoroughly familiar with peripheral vascular disease.

Slides illustrate the test with sodium nitrite to demonstrate the capacity of the vascular bed to dilate, the absence of reflex vasoconstriction in the sympathectomized limb and the technic of anterolateral extraperitoneal lumbar sympathectomy and of anterior apicolysis and thoracic sympathectomy. The indications and results of sympathectomy in selected cases of Raynaud's disease, Buerger's disease, poliomyelitis with vascular spasm and reflex dystrophy are shown in tables.

The conclusion is drawn that sympathectomy has a definite place in the treatment of a limited number of cases of peripheral vascular disease.

DISCUSSION

DR. LEWIS J. POLLOCK: Whatever benefit through sympathectomy may accrue to children suffering from the residual effects of poliomyelitis, it should be made

clear that sympathectomy cannot effect any amelioration of the paralysis, which is the result of lower motor neuron lesions.

Dr. G. de Takáts: I am grateful to Dr. Pollock for stressing what I thought I had made clear—that only children with vasomotor phenomena are subjected to sympathectomy, with no idea of influencing the paralysis. In looking over slides of the spinal cord of persons with poliomyelitis, I was interested to observe that they all show irritative lesions in the lateral horn or anterior roots; it may be that the vascular spasm originates there. There is no doubt, I believe, in any one's mind, that it would be useless to operate on children with a lower motor neuron lesion, except to relieve the vasomotor phenomena.

Liberation of Epinephrine and Sympathin by Stimulation of the Hypothalamus. Dr. H. W. Magoun (by invitation).

With the use of the denervated nictitating membrane of the anesthetized cat as an indicator, the liberation of circulating epinephrine and sympathin in response to stimulation of the hypothalamus was demonstrated.

A prolonged latent period and delay in the maximal contraction of the denervated membrane induced by these substances indicate that they are not responsible for the initial effects of hypothalamic stimulation on other organs. Their rôle in augmenting and prolonging hypothalamic effects, induced by direct nerve connections, is discussed; it is concluded that the influence of the hypothalamus in visceral innervation and emotional excitement is effected both by direct nervous influences and by humoral substances for the release of which these nervous influences were responsible.

DISCUSSION

Dr. R. W. Gerard: Two questions interest me particularly in this presentation. I wish to ask Dr. Magoun first whether he believes that the difference in time relations of the curves obtained with epinephrine, on the one hand, and with sympathin, on the other, would enable him to call them two different substances or whether the differences in rate of liberation or entry into the blood stream might account for the two time curves. Second, is there yet any evidence, either by excluding regions of the body from the circulation or by cutting their neural connections, as to the identity and relative importance of various organs for the liberation of sympathin.

Dr. M. G. Masten, Madison, Wis.: I shall report a case which I believe has a bearing on Dr. Magoun's research and may throw light on Dr. Gerard's question. A woman aged 41 presented symptoms of weakness on the right side for three months and reduced vision and vomiting for three weeks. Examination in the hospital revealed motor weakness on the right side and aphasic symptoms; the blood pressure was 210 systolic and 158 diastolic. There were exophthalmos and limitation of movements of the eyeballs in all directions. The disks were choked and measured 8 diopters; there were massive retinal hemorrhages and almost complete obliteration of arteries due to spasm. The clinical diagnosis was malignant hypertension. Postmortem examination revealed a tuberculoma, 4.5 by 4 by 4 cm., in the left thalamus, with softening of the surrounding brain. The adrenal glands (weight 32 Gm.) showed extensive tuberculosis, the medulla of the right gland being completely replaced by tuberculous nodules and the cortex being very thin. The left adrenal (weight 13 Gm.) showed the same process, but to a less degree.

This case suggests that the hypertensive syndrome resulted from involvement of the vegetative centers, and since adrenal function must have been eliminated by the extensive tuberculosis, it argues either for the elaboration of a hormone, such as sympathin, or a direct nerve connection between the cerebral visceral centers and the vascular system. Ordinarily, tuberculosis of the adrenals is marked by vascular hypotension.

Dr. H. W. Magoun: It is difficult to compare the time relations of contractions to what I have called epinephrine and sympathin in these experiments, because

those which recorded the liberation of epinephrine were made with a relatively nonsensitized membrane and in those recording the action of sympathin, on the other hand, the membrane was highly sensitized. I realize that the question whether epinephrine and sympathin are identical is controversial. Loewi and Bacq, on the one hand, believe they are identical, while Cannon and Rosenblueth are opposed to this view and have demonstrated differences in action which, so far as I know, cannot be explained on the assumption of their identity.

As all parts of the peripheral sympathetic system are excited from the hypothalamus I have assumed that sympathin liberated by hypothalamic stimulation has a widespread peripheral origin, but I have not performed section experiments to demonstrate this.

The case cited is an interesting one.

THERAPY IN CATATONIA: EFFECTS OF COMBINING CAFFEINE WITH SODIUM BENZOATE WITH SODIUM AMYTAL. DR. SAMUEL B. BRODER (by invitation).

Accidentally, I observed that the intramuscular injection of 7½ grains (485 mg.) of caffeine with sodium benzoate, followed by the intravenous injection of 3¾ grains (243 mg.) of sodium amytal, resulted instantaneously in apparently normal behavior of a catatonic patient. This observation led me to investigate the possibilities of employing this method therapeutically, since I have not found that catatonic patients respond well to *Dauerschlaf*. Having previously satisfied myself of the importance of psychotherapy coincident with the use of a hypnotic agent in the treatment of psychotic patients, I also applied intensive psychotherapy in this investigation.

Over 700 injections of caffeine with sodium benzoate and sodium amytal were administered to 16 patients and 16 normal persons. Of these over 350 injections were given to 8 catatonic patients and nearly 300 to the other 8 psychotic patients (3 with manic-depressive psychosis, 2 with hebephrenia, 1 with paranoia, 1 with psychoneurosis and 1 with an unclassified psychosis).

Physiologic changes, such as alterations in pulse rate, rate of respiration and blood pressure readings, were recorded before the treatment and at five minute intervals for twenty minutes after the administration of the drugs, but were too insignificant and irregular to merit emphasis.

The effect of the combination of caffeine with sodium benzoate and sodium amytal, when administered in certain quantities by certain routes, on mutism, rigidity, slovenliness and stereotypy of posture and speech in the catatonic patient is reported.

It is concluded that an intramuscular injection of 7½ grains (485 mg.) of caffeine with sodium benzoate, followed about ten minutes later by an intravenous injection of 3¾ grains (243 mg.) of sodium amytal in a 10 per cent solution, is beneficial in producing a change in mutism, rigidity, slovenliness and stereotypy in catatonia. The change may last from a few hours to a few days. Two catatonic patients who were subjected to this form of treatment recovered. No explanation of the cause for the favorable change is offered. There is no correlation between the number of treatments and the nature or duration of a favorable response.

DISCUSSION

DR. FRANCIS J. GERTY: I am always puzzled to know what to think of these experiments. They are an interesting approach to the patient; yet so far as I know none of the attempts has revealed much of the mechanism that induces the catatonic state. In the morning I have selected patients in typical states of catatonic stupor to demonstrate in the clinic in the afternoon, and when afternoon came, there was nothing of catatonic stupor left to demonstrate. Also, I have seen many patients who were believed, on fairly good grounds, to have had catatonic schizophrenia for many years and who later have appeared normal, with no evidence of mental deterioration. Work with these patients has not given me much impression as to the cause of the trouble. Possibly, Dr. Broder has made observations in regard to this of which he can tell.

PHILADELPHIA NEUROLOGICAL SOCIETY

Nov. 27, 1936

F. H. LEAVITT, M.D., *Presiding*

CENTRAL CONTROL OF SYMPATHETIC ACTIVITY AND THE RÔLE OF THE HYPOTHALAMUS. DR. D. W. BRONK, Philadelphia.

The development of electrical methods for recording the impulses in the sympathetic nerves makes it possible to study the activity of the centers in which these impulses originate and which control visceral activity. The present report deals mainly with an analysis of the discharge over the sympathetic nerves to the heart and blood vessels of the cat.

In the great majority of cases and under a wide variety of experimental conditions there is a "tonic" discharge of impulses. This, however, varies considerably and is profoundly modified by variations in blood pressure and depth of respiration. The maximum frequency of impulses from a single sympathetic nerve cell has never been observed to exceed 10 or 15 a second, which is decidedly less than the frequency of impulses generally found in the somatic nerves. This is in accordance with the difference in the frequency of stimulation necessary to produce a maximal response of the effector organs supplied by the two systems.

The synchronous discharge of large numbers of cells in volleys, varying from 1 every five or ten seconds up to about 20 per second, is characteristic of the sympathetic centers. Here again, there is marked contrast to the somatic system. There, such synchronized volleys would produce gross tremors; it is not so in the sympathetic system because of the slow response of the effector organs supplied by the sympathetic nerves. Frequently these grouped discharges are synchronous with the heart beat or the respiratory cycle, and then it can be shown that the periodic activity is due to the central effect of the volleys of impulses over the afferent nerves from the blood vessels and lungs. This control of the sympathetic centers by afferent impulses is illustrated by experiments in which large groups of cells are caused to fire synchronously by electrical stimulation of the central ends of various afferent nerves, such as the vagus and sciatic nerves and the branch to the carotid sinus.

In considering the regions of the brain stem responsible for this coordinated and reflexly controlled sympathetic activity, my colleagues and I naturally were led to investigate the rôle of the hypothalamus. By recording with needle electrodes, Lewy, Larrabee and I have been able to detect rhythmic activity in the lateral hypothalamic nuclei similar to that in the efferent sympathetic nerves; we have been able to drive the activity of the hypothalamus by volleys of afferent impulses and to initiate volleys of efferent sympathetic impulses by stimulation of the hypothalamus. This, then, is additional evidence of the rôle of the hypothalamus in the control of sympathetic functions. However, after removal of the hypothalamus the synchronized grouping of sympathetic impulses persists, and the discharge may still be inhibited reflexly by way of the afferent nerves. After section of the stem at the level of the fourth ventricle, the reflex control and grouping disappear, but there is still a continuous discharge of sympathetic impulses. We have been unable to modify this last type of activity except by asphyxia.

SIGNIFICANCE OF THE HYPOTHALAMIC REPRESENTATION OF THE SYMPATHETIC NERVOUS SYSTEM. DR. PHILIP BARD, Baltimore.

Dr. Bard discussed in some detail his own work and that of others on this subject.

DISCUSSION ON PAPERS BY DR. BRONK AND DR. BARD

DR. ERNEST SPIEGEL: I was particularly interested in Dr. Bronk's studies on the afferent part of the vegetative system. Dennig, who studied the speed of

conduction from the viscera, found no difference in the speed of conduction in the afferent vegetative fibers as compared with that in the somatic system. He concluded that the afferent fibers in the sympathetic system do not differ essentially from the afferent somatic fibers. The wonderful work of Bronk and his associates shows that one cannot generalize and that there exist definite characteristics of the centripetal vegetative impulses. Dr. W. C. Hunsicker Jr. and I were interested recently in the centripetal conduction of impulses from the bladder. We introduced a balloon into the urinary bladder and studied the conduction of the afferent impulses produced by distention of the organ. This produced changes in cortical action potentials similar to those with stimulation of other sensory nerves, showing that impulses from the bladder may eventually reach the cerebral cortex. In studying corticopetal conduction, the question arose as to whether these impulses have relation to the hypothalamus. The theory was advanced by Adler, on the basis of the anatomic studies of Wallenberg, that impulses from the bladder eventually enter the hypothalamus and from there, by the system of the fornix longus, reach the gyrus fornicatus. We studied the subject by destroying the afferent systems of the hypothalamus, stimulating the urinary bladder and making electrocorticograms. These experiments showed that intactness of the afferent systems of the hypothalamus is not necessary for conduction of impulses from the bladder to the cortex. In regard to the centrifugal impulses, I think that one of the first to stimulate the hypothalamus, long before Karplus and Kreidl, was Bechterew. This work was much criticized, and rightly, for if one stimulates the hypothalamus with an electric current one does not know whether one is stimulating ganglion cells in this region or corticofugal fibers that pass by the hypothalamus. I think the same criticism can be applied to most experiments of this type following those of Karplus and Kreidl. These authors were the first to study the effect of stimulation of the hypothalamus after degeneration of the corticofugal tracts, and only such experiments prove conclusively that ganglion cells of the hypothalamus have been stimulated.

As to the question of relation of the hypothalamus to the parasympathetic system, Lichtenstern, a urologist who worked with Kreidl in Vienna, described effects on the bladder. He observed contraction of the urinary bladder depending on the pelvic nerves and disappearing after severance of these nerves. These experiments showed that the sacral part of the autonomic system may be influenced by stimulation of the hypothalamus. As regards Cushing's work: in similar experiments on rabbits, i. e., intraventricular injections of small doses of pituitary extracts (*Arb. a. d. neurol. Inst. a. d. Wien. Univ.* **25**:247, 1924) I observed a fall of blood pressure, as did Cushing in his patients several years later. I was particularly interested in experiments on blood pressure which Dr. Bard performed after he had removed successive parts of the hemispheres. Dr. Yaskin and I destroyed first the cortex and then the optic thalamus and finally made a transverse section through the caudal part of the midbrain (*Ztschr. f. d. ges. exper. Med.* **63**:505, 1928). After each operation we stimulated the sciatic nerve and found something similar to that reported by Dr. Bard. After destruction of the cerebral hemispheres the blood pressure rose 54 mm. on sciatic stimulation; after extirpation of the thalamus, 60 mm., and after section through the caudal part of the midbrain, 90 mm.

I admire the way in which Dr. Bard showed the importance of hypothalamic centers for emotional reaction in chronic experiments. The question arises: What is the function of the hypothalamus? Has it functions other than regulation of temperature and emotional reactions? Nothing definite is known. Comparative anatomic studies (Roethig, Spiegel and Zweig) have indicated that certain parts of the hypothalamus (nucleus supra-opticus and nucleus paraventricularis) form a very old phylogenetic system. These nuclei may have something to do with integrations already represented in lower animals. What type of integration this is is not known. It is certainly not temperature regulation alone, for one finds such nuclei already in animals that have no constancy of temperature. The only working hypothesis I wish to express at present is that the hypothalamus may have

a coordinating function in regard to the lower segmental centers. What type of coordination this is I do not know.

DR. F. H. LEWY: The question of centers was brought up. It is an old controversy—whether what is stimulated in the hypothalamus are centers, i. e., an accumulation of ganglion cells, or tracts. It is a fight over words, and certainly, up to now, there is no possibility of differentiating centers and the tracts originating in them. The results of Ranson's experiments and those carried out by my co-workers and me have indicated that the spots by stimulation of which the pupillary reaction and carbohydrate, chloride and water metabolism can be influenced are fairly circumscribed. Histologically, these areas seem to correspond with various hypothalamic nuclei. It is my opinion that, in contradistinction to the vegetative vagus nerve, which innervates "organs," in the hypothalamus "functions" are represented. However, I have always believed that such functions should be considered of a more primitive nature than appears from the nomenclature.

DR. D. W. BRONK: So far as our experiments give me a basis for making a comparison, I am in entire agreement with Dr. Bard's opinion regarding the rôle of the hypothalamus in sympathetic activity. It undoubtedly exercises an important control, but after its removal many sympathetic functions appear to be unimpaired. The question raised by Dr. Spiegel is important. The concept of "centers" and their location is always difficult and often dangerous. Electrical stimulation and recording offer no easy resolution of these difficulties, for it is frequently not possible to distinguish between tracts and what is generally understood to be a "center." The frequently expressed opinion that slow electric potentials of brain tissue represent activity of cells rather than of axons is not justified. The summation of temporally dispersed axon potentials gives slow potential waves in every respect similar to those assumed to originate in cell bodies.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 1, 1936

THOMAS K. DAVIS, M.D., *President, in the Chair*

A SPECIFIC EPILEPTIC SYNDROME RELIEVED BY LYSIS OF PACCHIONIAN GRANULATIONS. DR. JOHN E. SCARFF.

This article was published in full in the ARCHIVES (**36**:373 [Aug.] 1936).

DISCUSSION

DR. FOSTER KENNEDY: I think there is no doubt that medicines could not have produced as good a result in the 3 cases that Dr. Scarff has described as he produced by his operation. The patient who for eighteen, thirty or forty years has had an increasing number of attacks, up to as many as several a day for months, is practically hopeless as regards the effects of medicines. Dr. Scarff has shown a type of epilepsy with a definite focal origin. The attacks had a definite focal beginning and then progressed to a generalized finish. For that reason instances of this type were chosen for this operation, out of the general mélange of cases of epilepsy. The fact that Dr. Scarff observed abnormal pacchionian granulations in these cases was a tribute to the selection of the type for operation. The result has more than justified the primary event—it has shown again that epilepsy is not a disease: It is a reaction. It is perhaps what fever is to infection, what perhaps many psychoses are—not primary disease units in themselves but reactions to other events of which little is known.

This operation, Dr. Scarff will be the first to say, is not the answer to the problem of epilepsy. It is the answer to a certain type of epilepsy, and it would

seem as sure as one can be from this limited group of cases that when epilepsy is long established—perhaps over almost a lifetime—and when it has had, if not in the present, then in the past, a definite focal origin—a focal emphasis, perhaps one ought to say, for it is not as definite as an origin—the condition is worthy of surgical exploration. The group to which I belong, at the Bellevue Hospital, have become almost "sloppy" as regards, for instance, diagnosis of spinal conditions. We have come to try to classify lesions of the spinal cord on the basis of whether or not the canal should be opened. If there is indication for opening the spinal canal, we think that our neurosurgeons are sufficiently skilful to do it, without risk. We believe that this is the proper attitude toward many spinal conditions. I will go further and say that this attitude of mind has been justified in the case of the brain by Dr. Scarff's results, even if in only 3 persons. If all the cities of the plain might be spared for one just man, surely these 3 cases are enough to spare one from therapeutic despair. This clinical picture is a definite symptom complex in epilepsy, in which there are many complexes. If one finds a definite signal symptom in the past history of the patient with epilepsy, even though it may have been "snowed under" by the time one sees the patient, the brain ought to be explored. The work of Foerster and Penfield and that done at the Bellevue Hospital for the past two and a half years by Dr. Scarff and Dr. Hausman have taught one much. These efforts are in a sense repetitions of former work, but they are repetitions by much better methods than were known in the days of the fathers, who were also interested in electrical stimulation of the cortex. Much better results are being obtained now (local anesthesia is of aid in surgical procedures on the brain)—results that will show what many have believed: that the brain is an enormous integration of centers and that there is no such thing as the brain working as a whole. It seems to work as a whole merely because it is beautifully integrated, so that one thing can be done at a time. The cortex does that. The more one carries out experiments, the more one finds that a center exists for each extraordinarily minute function. I shall refer to a letter just received from an old friend, Dr. Kinnier Wilson, concerning another matter. We had been talking back and forth in letters about medical and neurologic matters, and at the end of the letter he put this query: "A patient has his head open on the table and is conscious; when the electrode makes his arm or leg move, can you tell me whether he himself then thinks that *he* had made the movement? Does the movement then feel to him exactly the same as though he had willed the movement himself, or can he spot some difference; and if so, what?" That is a vital question. At the Bellevue Hospital yesterday, I found on the table an exceedingly intelligent young engineering student, who had had epilepsy for many years and who has an acute, clear and analytic mind, with good power of expression in speech. My associates and I asked him for a clear subjective and objective analysis of his experience on the table; he therefore had his mind "set" to the task. We asked him in as careful words as we could devise what he felt, what he experienced and how he himself was concerned when Dr. Scarff was stimulating his cortex. Did he feel that he had made the response himself? He thought carefully and said "no." Then we gave him the problem in which we had stimulated the brain and there was a latent period before the arm or leg moved. During that latent period, after the stimulation, had he the faintest adumbration that his arm or leg was going to move or that he himself was throwing, or was about to throw, the switch of his will, as it were, into the arm or leg? After careful thought he said "no." He said it was just as though the stimulation were being done "on the arm," i. e., on muscle motor points with the faradic current. There was in this patient, at least, a peculiar distinction between stimulation by the will and artificial cortical stimulation, and that is the answer to Dr. Kinnier Wilson's question. There is a clear subjective distinction between exogenous stimulation of the cortex producing a certain result and the will (whatever the will may be) affecting the same centers and producing the same result. This is a question of the relation of the person to the center and of the center to the person—probably the most

important problem in the world. The questions that Dr. Scarff has been helping to solve are good not only for the treatment of epilepsy but for the interpretation of life.

DR. BYRON STOOKEY: Dr. Scarff has called attention to a limited group of cases, as he said, which he has culled from the general group of cases of convulsive seizures. In the cases reported there were such definite initial jacksonian symptoms that even though they were "snowed under," as Dr. Kennedy stated, I think they warrant exploration of the area obviously involved. Dr. Scarff has had the good fortune to work with Dr. Kennedy, as I have in the past, and has profited by his willingness to explore an obscure lesion. The lesions observed at operation in these cases have well merited the exploration. However, as I know Dr. Scarff, I think he is too critical a surgeon to be as yet entirely satisfied with the results he has obtained. I should hesitate to consider them end-results. Dr. Scarff pointed the way for further research in the same field. Exploration, I think, is indicated when this particular syndrome is found, and such conditions should be dealt with as Dr. Scarff has suggested.

DR. H. A. RILEY: Were these patients receiving treatment before operation?

DR. JOHN E. SCARFF: Yes, I neglected to state that they all had been given phenobarbital and had received therapy for years; during our period of observations in the ward, they were receiving phenobarbital.

DR. H. A. RILEY: After operation did they receive phenobarbital?

DR. JOHN E. SCARFF: After operation they continued to receive the same amount which they had been getting before.

DR. H. A. RILEY: One other point occurred to me in connection with Dr. Kennedy's statement about the difference of appreciation of the willed and the stimulated movement. This does not seem to be strange, since I believe that no incentive to stimulation resulting in movement arises in the precentral cortex. In the process of stimulation by the electrode, one stimulates this area directly; the stimulation is therefore almost as abnormal as if the muscles themselves were directly stimulated. One does not stimulate the ancillary and the surrounding areas, which under ordinary circumstances give rise to movement. There is no stimulation in the sensory areas, from which the incentive syntheses are advanced to the more strictly motor areas, which then produce movement. There is no stimulation in the precentral region which would result in a skilled act or in an organized movement of a limb, or a large segment of a limb; so I think it is natural to anticipate, as is the fact and as Foerster said in his report of the cases in which there was stimulation, that the patients do not feel as though they were moving but as though they were being moved. I believe this is the case, for the stimulation is applied to the immediate motor areas rather than to the physiologic regions activity in which usually results in movement.

THE HUMAN ELECTRO-ENCEPHALOGRAM IN HEALTH AND IN CERTAIN MENTAL DISORDERS. DR. HALLOWELL DAVIS and PAULINE A. DAVIS (by invitation).

The human electro-encephalogram shows characteristic patterns associated with certain physiologic states. Among these patterns are the high voltage waves of grand mal and petit mal epilepsy; the large, slow, irregular waves of early sleep or unconsciousness, and the 14 a second rhythm of sleep.

Many persons show a regular 10 a second alpha rhythm, which is suppressed by visual activity, attention, sleep and other factors, but even under the most favorable circumstances other persons consistently do not show it. The pattern for a given person is constant in this respect. Identical twins show closely similar patterns. Our preliminary studies suggest an important hereditary factor.

A control group of 100 "normal" adults shows an even distribution between plentiful and scarce alpha rhythms. Seventy patients in the McLean Hospital (for the care of mental diseases) showed a preponderance of scarce alpha rhythms.

This is partly because arteriosclerosis and senility seem to be associated with low voltage or scarce alpha waves, or with their absence, but that does not entirely explain the preponderance. The group of patients suffering from manic-depressive psychosis show a nearly normal distribution. The patients with schizophrenia, on the other hand, show a significant trend toward scarcity of alpha waves. There is, however, an equally good correlation with the condition of the patient, irrespective of the diagnosis. Quiet and cooperative patients as a group show a nearly normal distribution of patterns, but the chronic or disturbed patients show a scarcity of prominent alpha waves. A few disturbed or chronic manic-depressive patients do show them, but so far we have seen them in only 1 chronic schizophrenic patient.

We are continuing our investigations to determine whether an underlying hereditary factor determines these distributions, and to what extent the degree of mental disturbance, irrespective of clinical diagnosis, may influence the patterns.

PRACTICAL AND THEORETICAL SIGNIFICANCE OF THE ELECTRO-ENCEPHALOGRAM IN EPILEPSY. DR. FREDERIC A. GIBBS and DR. WILLIAM G. LENNOX (by invitation).

We believe that epilepsy is caused by a defect in the mechanism which regulates the rate and amplitude of the electrical fluctuations of the brain. Three abnormalities in rate are possible: Activity may be too fast or too slow or may oscillate between fast and slow. Abnormalities of frequency are associated with abnormalities of voltage. Attacks of grand mal are characterized by fast waves; psychomotor outbursts, by slow waves, and petit mal attacks, by a rhythmic alteration between slow and fast waves. There are characteristic frequencies and wave formations for each of these three types of seizure.

The effect of sedatives, carbon dioxide, sensory stimulation and many conditions which precipitate or prevent seizures is related to the changes produced in the rate of cortical activity. Electrical studies show that seizures may sometimes start as petit mal and end as grand mal, or the reverse. So, also, frequencies and wave formations characteristic of a psychomotor outburst may precede what is, both electrically and clinically, a grand mal or a petit mal attack. Whether the patient will have any symptoms and the particular symptom experienced depends on: (1) the frequency and voltage of the fluctuation in potential; (2) the duration of the burst of pathologic activity, and (3) the parts of the brain involved in the disturbance. In the between seizure record of patients with epilepsy, abnormalities of rate and amplitude are often observable. In 1 case that we have studied extensively, the ratio of two types of abnormal waves in a fifteen minute record affords a reliable basis for predicting grand mal seizures one day in advance. Under increased medication with barbiturates and bromide, the localized disturbance which warns of this patient's seizure is not altered, but no seizure occurs with an amount of pathologic activity that without medication would certainly have been followed by a seizure. This seems to indicate that sedative drugs prevented seizures in this case not by stopping the original disturbance but by preventing its spread.

DISCUSSION

DR. HERBERT S. GASSER (by invitation): These papers on the changes of electrical potential give an idea of the rapidity of advancement of this subject during the few years of its existence. From these studies made on man, as well as from studies of other investigators on animals, one has now a general picture of the electrical oscillations which seem to go on continuously in the cortex. After looking over the records of various observers, one is prepared to accept the point on which Dr. Davis insisted at the beginning of his lecture, that the waves represent a fundamental process in which certain features recur regularly. One has some idea of the variation of the waves in the different cyto-architectonic fields and of their relation to the different layers of the cortex. One knows

something about the modification of the waves by the arrival of afferent impulses at the cortex and the changes occurring between the states of sleeping and waking and in narcosis. There has also been provided information about the mode of spread of excitation through the cortex. Finally, these papers show how the waves vary from person to person and appear in new characteristic forms in disease.

There is being developed a new branch of electrophysiology dealing with neurons in the aggregate. Like all new developments, it brings with it a series of new problems. It is natural that the first stage should be descriptive; it may be expected that this stage will give way to a second stage devoted to the solution of the problems which have been brought to light. For example, one can well believe that the "spike and wave" variation of the potential, of which Dr. Gibbs and Dr. Lennox have spoken, may represent the end-result of a more deep-seated disturbance. If the promise which is held out for this new branch is really to be fulfilled, it must be correlated with the older branches. If the cortical potentials are to be interpreted, one must know how they are produced—the configuration of the potential change during activity in the individual neurons and the mode of propagation through the complex pathways provided in the neuron chains. Do these waves represent the rise and fall of potential in individual neurons, or are they kept up by transmission of excitation over closed chains of neurons? Are they made up of long potentials or of numerous short potentials out of phase? These are questions to which there are no definite answers, but they are questions which must receive answers if the older branches of electrophysiology are to be of use to the new branch. The challenge which the observations reported here gives to one's powers of explanation is timely because of the directive influence which it will have on future research.

DR. BERNARD SACHS: The subject is so new I think it would be foolhardy for those who have not, and probably never will, become thoroughly acquainted with the method to say much. It is distressing to me to hear that, in addition to all sorts of other patterns, all persons are evidently built according to certain electric patterns. Can any one tell me whether these electric patterns remain the same from week to week, from month to month and from year to year, or whether they change? Is the electric pattern different whether a person is thinking or not and whether he is engaged in any mental activity at the time, or is it something which is independent of general cerebral activity? That is the only thing which has occurred to me: Is this electric pattern something one is born with? I dislike to think that one is born with a special kind of electric pattern, which perhaps does not change essentially throughout life. So much is suggestive in these presentations that all I can say is that I am happy to have lived long enough to hear of the electro-encephalogram and all these facts about the electric activity of the brain. It is a promising field, and I shall be glad to be advised of further advances in it.

DR. FOSTER KENNEDY: These records of identical twins are about as remarkable as anything to be seen at a medical meeting: identical Berger readings, in persons with identical faces and identical behavior. But one rather loses sight of the mysteries that are under one's nose, and like the Pharisees, one runs after a new thing because it is new. These graphs, for all their strangeness, are truly not any more remarkable than the fact that nearly all the people in the world have a pulse rate of 72, a water balance of 50 ounces (1,363 Gm.), a respiratory rhythm of 18 or a sleep rhythm of one third of their lives. These also are really important mysteries, and there is not an iota of knowledge on how they are determined; they must depend on such rhythms as these shown here. One is so accustomed to the common rhythms that one pays little attention to their physiologic significance; they are accepted like sun, moon and stars.

A man, perhaps, is a kind of coagulum or knot in a stream of energy, with a momentary opportunity for experience. He is subject to the rhythm of the uni-

verse—a pulse indeed. The alliance of physics and medicine is no longer just a verbal play—research in one grows to be research in the other.

DR. S. BERNARD WORTIS: I wish to ask Dr. Davis whether he believes that brain rhythms are a measure of cerebral integration and whether they have any relation to the personality or the constitutional type in the normal persons he has studied.

DR. GEORGE V. N. DEARBORN: I have long been convinced that some "hysterical" convulsions are undifferentiable from the perhaps atypical "epileptic attacks, and I wish to ask Dr. Davis and Dr. Gibbs whether they have any suggestions as to the conditions and forms of the rhythmic action currents underlying some of these occasional hysterical seizures.

DR. E. D. FRIEDMAN: One can only express great admiration for the type of research applied to clinical medicine which has been presented here. I am intrigued by the confirmation of the importance of the constitutional factor which the work of Dr. Davis and his co-workers has emphasized. It is interesting to hear confirmation of the theory of the rhythmicity of discharge of the pyramidal and other tracts; there has been postulated an automatic rhythmicity of discharge of the pyramidal tract at the rate of 10 or 12 per second; this seems to be borne out by the rhythmicity of the electro-encephalograms shown.

It is also interesting to hear from the experimental side confirmation of the clinical fact that physicians are better able, by means of sedatives, to control grand mal seizures than attacks of petit mal. I am also glad to note that the various forms of mental disease have graphs of their own. While there may be a certain temerity in attempting to stigmatize persons with labels such as manic-depressive psychosis and schizophrenia, for the line of division between various forms of mental illness is often thin, yet in the main this differentiation seeme to be borne out by some of the work presented by Dr. Davis and his co-workers.

MRS. HALLOWELL DAVIS: One feature which is perhaps noteworthy in the patterns of the patients studied at the McLean Hospital is the greater variability of frequency and of voltage shown by the patterns, and in this they differ from those in normal series.

DR. HALLOWELL DAVIS: I cannot take up all the various comments that have been made, but there are one or two points which I shall discuss. Dr. Gasser's challenge concerns the physiologic interpretation of the activity of neurons in the aggregate, and what it means. I appreciate the full force of that point. Some of my associates, Dr. Forbes in particular, are taking up that challenge, and I hope that Dr. Gasser will join in the pursuit himself and give us the benefit of his wisdom and experience.

As to the constancy of pattern, the method is not old enough to answer that question entirely. We have been recording these patterns for not more than two years, and therefore we cannot yet say whether a pattern is constant year after year. We can say that it is constant when we study the same person under comparable conditions week after week and month after month. It is true that a child does not start off with the full-grown adult pattern. He begins with a slower rhythm, which gradually speeds up and attains its adult form at about 10 years of age. We do not know whether the distribution of types at that stage is the same as among adults, that is, whether every 10 year old child has fallen into a type in which he will remain from then on. That is an interesting point on which we hope to secure data soon. Of course, one can stop the alpha rhythm temporarily, as by opening the eyes. We have found practically nothing which will modify the beta waves, and so we can give only incomplete answers to that question.

DR. FREDERIC A. GIBBS: I may add, in answering Dr. Sachs' question, that persons with epilepsy do show an extreme variation in their brain rhythms from month to month and from day to day. Dr. Davis, who has studied normal subjects and patients with various types of mental disorder, reports a greater constancy

than we have seen in persons with epilepsy. In epilepsy, something is wrong with the "governor" which regulates cortical rates. This lack of normal regulation of rate is, we believe, characteristic of epilepsy.

Concerning Dr. Dearborn's question about hysterical seizures, we cannot say much, for we have found that when we lead off from the wrong place, we may often fail to see any pathologic activity. For instance, in certain cases of petit mal a movement of the electrode of 3 cm. will show that at one place one can get many large waves and spike formations, and at another, apparently normal activity, so that we are not willing at present to say that because we cannot record typical seizure waves during a seizure, the patient is hysterical or malingering. All we can say is that in such patients we cannot pick up from the outer surface of the cortex any abnormal activity. This may mean that there is no abnormal activity such as occurs in epilepsy, or it may mean that the abnormal activity does not involve the part of the brain from which we are leading off.

Book Reviews

A Study of Hypoglycæmic Shock Treatment in Schizophrenia. A Report. By Isabel G. H. Wilson, M.D. Price, 1 shilling, 3 pence. Pp. 74. London: His Majesty's Stationery Office, 1936.

This monograph, in the form of a report to the Board of Control of England and Wales, presents the observations, conclusions and recommendations resulting from an investigation in Vienna of the treatment with hypoglycemic shock of nine male and thirteen female patients with schizophrenia, together with a review of the opinions of other psychiatrists in Vienna and the available literature regarding the treatment. Wilson also saw eight patients who were receiving treatment at the Münsingen Hospital for Mental Diseases in Bern, Switzerland, under conditions very different from those in Vienna, and studied the histories of thirteen patients treated formerly in other Swiss hospitals for mental diseases.

The report contains chapters devoted to the treatment in detail, the mental effect and management, the difficulties, danger and theories of the treatment and a discussion of the results, conclusions and recommendations, together with a bibliography and a useful appendix containing instructions for nurses, from the Münsingen hospital.

Sakel's original plan was to produce states of shock which his predecessors had sought to avoid as disturbing and dangerous. The technic is as follows: Intramuscular injections of insulin are given daily at 7 a. m. to patients in a fasting state. No food is given for from four to six hours after the injection. There is an introductory phase during which the patient is more or less tested out, the dose being increased day by day. The second phase is accompanied by the symptoms of shock. Sweating is marked; a dry skin during shock is regarded as prognostically unfavorable. Hunger is often complained of before somnolence sets in. Rarely, there is a "hunger riot," during which the patient shouts and struggles to obtain food; in such cases food must be given at once. Bradycardia during the actual shock is consistently present. If the pulse increases rapidly in rate and becomes small or thready, Sakel believes that the normal action of insulin is being overcome by a toxic effect and advises that shock be interrupted. Drowsiness or coma almost always occurs and varies in depth. When corneal reflexes disappear, the patient is considered to be in coma. Loss of the light reflex of the pupil is usually regarded as an indication for the interruption of shock. The patient may be left in coma for varying lengths of time, up to two and one-half hours. Muscular twitchings, stretching and vague movements of the arms and legs are common. An epileptiform attack may occur at any time between the onset of hypoglycemia and full awakening, and is an indication for immediate interruption of shock. Laryngeal spasm is uncommon, but if there are stridor and cyanosis a nasal tube should be inserted. If impairment of respiration lasts for any length of time, shock should be interrupted.

The treatment after waking is of the utmost importance. If the patient awakens after a feeding, he is often restless for a few minutes. Sakel speaks of the disappearance during shock and the return on waking of cerebral function, level by level, and describes aphasia and retrograde amnesia. Many patients have amnesia for the period from obvious onset of hypoglycemia until waking. This accounts for their cheerful acceptance of a treatment which during the hypoglycemia is often distressing both to them and to the onlooker. There is danger of "after-shock" if the patient is allowed to sleep indefinitely or to miss the midday meal. The patient is allowed to occupy himself as he chooses after his meal and to enter into light occupations.

The dose is extremely variable. Severe shock may develop from 30 units in some cases; in others as much as 245 units is not sufficient to produce shock. The experience in Switzerland is that from about 100 to 200 units is necessary in new, untreated conditions and that in those of long standing the requirement is about 20 units. In all the hospitals investigated, the average dose required to produce shock was from 60 to 80 units. The blood sugar rarely falls below 40 mg.

The technic for the interruption of hypoglycemia is to give from 150 to 200 Gm. of dextrose in tea, milk or water. Nasal feeding is commonly used in Vienna. Gastric studies have been made, and hypersecretion of gastric juices is constant. If the interruption is due to an emergency, dextrose is given intravenously. The waking from intravenous injection of dextrose may be dramatic. Subcutaneous injection of a few drops of a 1 : 1,000 solution of epinephrine hydrochloride is the quickest means of beginning to counteract the effect of insulin. If vomiting occurs, atropine sulfate, in doses of from 10 to 15 drops of a 1 : 1,000 solution, may be given by a stomach tube. Dussik and Sakel have listed eighteen items necessary for a complete apparatus for interruption. Interruption seems to be indicated: (1) when the hypoglycemia is considered on therapeutic grounds to have lasted long enough; (2) in the presence of a poor or rapid pulse; (3) when an epileptiform attack occurs; (4) in the presence of laryngeal spasm, and (5) on the appearance of a variety of complications, such as depression of respiration, pallor or cyanosis.

One of the most striking effects of the therapy is the occurrence of lucidity. Wilson observed a number of dramatic instances of temporary clearness and insight. Theoretically, in a case in which progress is favorable the lucidity of the hypoglycemic condition becomes gradually prolonged until the normal periods coalesce and the patient is free from symptoms. Psychotherapy and friendly encouragement are employed in this phase by Müller, in Switzerland, and Sakel, in Vienna. This superficial form of therapy is recommended, and avoidance of deep psychic probing is encouraged.

Three of the first one hundred and four patients treated in Vienna died. There were no deaths among forty-one patients treated in Switzerland. The importance of careful physical examination is stressed. Epileptiform seizures denote a serious effect of insulin. Repeated epileptiform attacks are to be avoided. Damage to the pancreas is questionable. Gain in weight and changes in sugar metabolism are to be expected, and sometimes the gain in weight is large. "After-shock" is a danger not to be overlooked. In the avoidance of this danger the insulin should be given early in the day, and adequate carbohydrates should be given by mouth. The body temperature is usually subnormal, and it is important to make the patient warm and dry after the treatment. Aspiration of saliva and other materials is to be avoided.

Sakel seems to think along the following lines: Reactions of the nerve cell to stimuli run along definite conduction paths. When a healthy, young path is destroyed by a noxa, the reaction is compelled to run along an already disconnected or deformed path. If one can succeed in holding back the exciting substance from the cells by blockade, an opportunity may be given the cell to recover and become healthy. The therapeutic effect then, according to Wilson, may work somewhat as follows: saturation of the exciting substance and blockade of the nerve cells. By this means the stimulus is kept from the pathologically reacting cell, and time and opportunity are given it to polarize the normal conduction path.

Sakel and his collaborators speak of a specific effect of insulin in inhibiting that which is functioning (the psychosis) and in activating that which is latent (normality). Müller points out that it is not known whether the mental manifestations of hypoglycemia in the psychotic person are a real emergence of psychosis under the influence of insulin or merely effects which can be observed in normal persons in response to insulin. Sakel also points out the element of shock in the therapeutic effect. Perhaps every conduction path not yet firmly fixed may be destroyed, and on recovery the original normal conduction paths may predominate and can easily be polarized in the normal direction through further treatment. Sakel proposes a possible detoxicating effect on the body as a whole by influencing the basal metabolism. Professor Berze proposed a theory of *Emotionstherapie*—"probably nothing more is concerned than psychic trauma or emotional shock bound up with insulin treatment."

The average duration of stay in the hospital was from three months to one year. Relapses are not common and can be overcome by repetition of the treatment.

There are an excellent bibliography of one hundred and two references and an appendix containing a list of names of those who contributed to the study. The

monograph is an excellent summary of the practical technic and represents an abstract of the literature on the subject to date. It is adequate as a guide to the management of treatment with insulin shock.

Theoretische und experimentelle Studien zur Methylenblaufärbung des Nervengewebes. Heft 1. Acta morphologica. Arbeiten aus dem morphologischen Laboratorium der Filiale des Institutes für experimentelle Medizin (WIEM) und dem Staatlichen anatomischen Institut in Gorkij (UdSSR.). By Prof. Dr. Arnold Schabadasch. Price, 3 rubles; bound, 4 rubles. Pp. 244, with 24 illustrations. Gorkij: State Publishing House, 1935.

In this monograph, divided into three chapters, the author discusses in great detail the principles underlying the famous methylene blue (methylthionine chloride) staining method introduced by Ehrlich fifty years ago. It is also known as the vital staining method, for one of the prerequisites for successful staining laid down by Ehrlich was the living condition of the tissues. Schabadasch justly points out that the staining methods used generally for research or other purposes are for the most part empirical procedures. Theoretical considerations underlying the rationale of the staining methods are usually ignored. Such an attitude, of course, is a great detriment to science, for often only knowledge of the theoretical principles may lead the way to rendering a method workable, even in tissues to which ordinarily they are not applicable. The correctness of such views was splendidly proved by Schabadasch, who studied the principles underlying the methylene blue staining method in more than one hundred and sixty experiments on staining in a great variety of animals, including cold-blooded forms. He came to the conclusion that Ehrlich's views concerning the preponderant rôle that oxygen and alkalinity play in the success of the staining must be modified. He found that the success of the method is due exclusively to the hydrogen combination ("hydrogen acceptors") and the low alkalinity (p_H less than 7). He definitely proved that methylene blue produces profound chemical changes in the tissues with which it comes in contact. It affects the carbohydrate metabolism, causing "glucolysis" or acidosis. He also found that the staining is favorably affected by factors stimulating such metabolic changes and vice versa and that the tissues generally stain much better when the solution of the dye is combined with certain chemicals (resorcinol, paraphenylenediamine, sodium bromide, magnesium bromide and others). The results of the staining of various nerve plexuses (in the intestines, the gastro-intestinal mucosa, the uterus, etc.) are pictured in twenty-three splendid photomicrographs. The stained tissues can be studied under a high power lens (× 1,200) without previous fixation in formaldehyde, embedding or sectioning. Schabadasch calls his method "spatial microscopy" (Raummicroscopie). The results obtained by this method are discussed in great detail from various angles (physical, chemical and physiologic). It is a splendid contribution to the understanding of a staining method which has served so greatly to advance knowledge of the anatomic structure of the peripheral and the sympathetic nervous system.

Mental Nursing Simplified. By O. P. Napier Pearn, M.R.C.S., L.R.C.P., D.P.M. Second edition. Price, $2. Pp. 328, with 23 illustrations. Baltimore: William Wood & Company, 1936.

The first edition of this book appeared in 1931. The revised edition contains new material and has been distinctly improved. The contents are well organized, and the facts are stated with clarity and simplicity. The book being an English publication, the terminology is different in many instances from that in use in the United States. The author states as the aim of the book "to prepare students to pass examinations." To prepare students adequately to meet situations they must face in their daily work seems a more appropriate aim. The book is well adapted for quick reference by nurses and as a good textbook for attendants, but it has little value as a text or general reference book for persons preparing for professional nursing. It is too elementary for this purpose and includes none of the principles underlying the nursing technic given.

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